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TUMOUR CELLS AND THEIR SPREAD*

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CANCER KILLS by interfering with the normal physiology of vital organs. Local tumour growth can often be eradicated by one or several therapeutic modalities, but the treatment of discontinuous, distant metastases is still ineffective. Information about the spread of tumour cells is important both for proper clinical decisions concerning treatment and for suitable application of regional or systemic cancer chemotherapy.

ROUTES OF SPREAD

As late as the nineteenth century, some pathologists thought that cancer spreads by releasing "humours" which transform normal cells or embryonic rests into malignancy. Further studies, however, led to the modern concept of spread by means of cells and clumps of cells derived from the primary tumour.

The Lymphatics

Interest first centred on the role of the lymphatic system, probably because of the frequency with which involvement of the regional lymph nodes is associated with the growth of a tumour mass. Besides, advances in surgical and radiological techniques made treatment of the invaded regional tissues feasible, and the patterns of the lymphatic spread of malignancy of practical importance.

Tumour cells caught in lymph nodes die, become dormant, or grow into established metastases. The crucial factors resulting in survival or death of such tumour cells include real but ill-defined host resistance factors and the vitality or ability of the malignant cells to survive when separated from the mother growth.

Certain kinds of tumour cells appear to spread chiefly by means of the vascular system, and certain others by means of the lymphatics. The monograph by Willis[1] is an excellent source of information on the spread of tumour cells in the lymphatic system.

We[2] have endeavoured to obtain information in regard to the numbers of tumour cells entering the blood vessels directly as compared with the numbers of those entering the blood through the lymphatics and the thoracic duct. Polyethylene catheters have been placed in the left thoracic duct at its entrance into the subclavian vein. Of 50 patients with advanced malignancy, 11 had tumour cells in the lymph of the thoracic duct. Large numbers of abnormal cells and cell clumps were found in patients with lung or stomach cancer, but none in those with carcinoma of the colon and rectum, even though peritoneal carcinomatosis and liver metastases were present. The isolated malignant cells were counted or cultured or both, and were used to assay their sensitivity to various chemotherapeutic agents both *in vivo* and *in vitro*.

The Blood Stream

Sporadic reports of large atypical cells in blood smears from patients with advanced malignancy have been made since 1869.[3] The spread of cancer cells as emboli in the blood stream was associated with the development of pulmonary and liver metastases, but most metastases were thought to have resulted from spread through the lymphatics. Even in recent years, there have been statistical studies purporting to demonstrate the occurrence of metastases to distant ipsilateral organs by way of the lymphatics, e.g. lung cancer spreading to the adrenal and kidneys. It is still taught that liver metastases from breast cancer result from the spread of cells in lymphatics penetrating the rectus muscle and its fascia, the diaphragm, and on into the liver.

The first systematic search for tumour cells in the blood was made by Pool and Dunlop[4] in 1934. They hemolysed the erythrocytes, concentrated the remaining cellular elements, and prepared sections of this material. Abnormal cells were obtained from 17 of 40 patients with advanced cancer.

In 1955, Engell[3] reported isolation of tumour cells from the peripheral blood as well as from blood samples taken during surgery from veins draining the tumour site. Of 79 samples of peripheral blood from patients with carcinoma of the

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colon and rectum, 10 contained tumour cells. There were single tumour cells and cell clumps in more than 50% of the blood specimens obtained from veins directly draining the primary tumours. Since 1957, many clinics have reported the identification of tumour cells found in blood samples. Various separatory techniques have been used, such as sedimentation and centrifugation,[5, 6] sedimentation and flotation,[7] hemolysis and centrifugation or filtration,[8] and the older method of embedding and sectioning the buffy coat.[3, 9]

Research groups in Canada have reported similar studies, such as those of Romsdahl *et al.*[10] on malignant melanoma, those of Salgado and his associates,[11] and the study of exfoliated brain tumour cells by Morley.[12] We are aware of many other studies from your various Annual Reports. Similarly, there are several reports from England, a few from continental Europe, and numerous ones from Japan.

It is immediately apparent that the results of these various studies cannot be compared directly. Not only are there differences in isolation techniques and diagnostic criteria, but also varying numbers of divers kinds of tumours are included, as well as patients with varying degrees of malignancy.

In our laboratory, sedimentation of the red blood cells is accelerated by the use of a heparin-fibrinogen mixture. The plasma layer is separated and centrifuged at 1000 r.p.m. for about 10 minutes. The packed cells are re-suspended in a minimal volume of plasma, and heavy smears are prepared. Wright-Giemsa staining is our preference. The Papanicolaou technique is equally satisfactory if one takes the time to learn the cytological appearance of hematological elements, including immature forms. Examining each smear preparation with a low-power objective takes about 15 minutes. Usually three slides are prepared from the buffy coat obtained from each 5-ml. blood sample.

Tumour cells are generally recognized on the basis of their large size, disproportionately large nucleus and nucleoli, and "immature" chromatin pattern. The average diameter of cancer cells in smear preparations was about *19 micra*.[13] There is little doubt, however, that small tumour cells may escape detection, since screening is performed with the low-power objective. Thus the number of tumour cells identified represents a minimum frequency.

Of particular interest is the study of blood samples taken at the time of operation from veins directly draining the tumour site. Blood samples are likely to contain tumour cells and cell clumps to the same extent as tissue sections reveal invasion of blood vessels by tumours. Tumour cells have been found in blood samples from 80% of surgical patients with lung cancer, 50% of those with gastric cancer, and 30% of those with carcinoma of the colon and rectum. These findings parallel reports of venous invasion in similar patients by various investigators. Positive blood samples from regional veins were obtained from 16% of the patients with resectable colon lesions, and from 37% of those with non-resectable lesions. Regional blood samples were slightly more often positive after surgical manipulation, and usually contained greater numbers of cells and cell clumps per sample.

Probably a majority of the tumour cells released into the blood stream are "caught" in successive capillary beds. Nevertheless, the peripheral blood may contain cells 40 *micra* in diameter, and even larger clumps of cells.[13] This observation is ample evidence that some cells can pass through capillaries by deforming their shape, or can circumvent the capillary barrier by means of shunts between veins or between arteries and veins.

FATES OF EXFOLIATED CELLS

There is little doubt that 95 to 99% of all cells released from a primary tumour are promptly destroyed. Roberts and his colleagues[7] took serial blood samples in the course of operations and noted an increase in the numbers of tumour cells in both regional and peripheral blood during surgical manipulation of the tumour site. The disappearance of the abnormal cells within minutes after ligation of the blood supply to the tumour was remarkable. Such studies give significant evidence of the clearance of tumour cells from the blood.

Even patients with advanced tumours have a relatively small number of metastases in comparison with the number of malignant cells that can be recovered from the blood and the lymph. An occasional patient with malignant melanoma demonstrates the situation which might be found if the majority of exfoliated tumour cells were capable of sustained growth. Such patients may have literally thousands of individual metastases in all tissues of the body. In contrast, when volunteer patients with advanced disease are subjected to reimplantation with their own tumours, the transplantations are rarely successful, perhaps reflecting host resistance.[14] Certainly these evidences of host resistance, as well as the phenomenon of dormant tumour cells, deserve further study.

SITES OF METASTASIS

The Body Cavities

Cancer cells are exfoliated into the spinal fluid[15] and the pleural[16] and abdominal[17-20] cavities. The frequency of exfoliation varies greatly, depending on the kind of tumour. For example, over 90% of all deaths from ovarian cancer are actually due to carcinomatosis of the peritoneal cavity without distant spread.

In the Roswell Park clinic, the peritoneal and pleural cavities are routinely washed by spraying the viscera with 20 ml. of saline, and the fluid is recovered for study. The fluid is centrifuged, and smear preparations are made. Washings are done both before and after excision of the tumour, but there is generally little difference in the frequency

of positive smears. (As might be expected, sampling errors are considerable.) In several instances in which a malignant cyst was ruptured, or a raw surface of a tumour was exposed during surgical manipulation, subsequent washings contained tumour cells. In general, the frequency of positive washings paralleled tumour types, serosal invasion, blood-vessel invasion, and the presence of metastases.

The Bone Marrow

Many clinicians have observed tumour cells in the bone marrow. In 1958, we reported a series of 305 cases in which both peripheral blood samples and sternal marrow aspirations were taken.[21] Surprisingly enough, although the frequency of abnormal cells was about the same (8%) for both bone marrow and peripheral blood, there were only a few instances in which both were positive. It should be pointed out that accurate diagnosis of single cancer cells in marrow preparations is difficult. Positive diagnosis in these cases was based on finding clumps of malignant cells. Thus these findings in the blood and bone marrow are not truly comparable.

LABORATORY STUDIES

In the laboratory, model experiments can be utilized to investigate the phenomena of cancer-cell spread. It must always be kept in mind, however, that laboratory tumours growing in inbred animals are not strictly comparable to clinical situations. The intravenous injection of nearly a million ascites cells may result in the establishment of only a few pulmonary metastases, and yet it can be proved that large numbers of tumour cells were distributed to most organs.

One of the most interesting areas of cancer research should be the study of the differential destruction of tumour cells in various organs. For example, we have never observed a brain metastasis in thousands of mice into which large numbers of various tumour cells had been injected intravenously, and yet only one or two cells are necessary to establish intracranial growths when they are injected directly into the brain itself.

At present, we can affect tumour-cell distribution by interfering with the reticuloendothelial system, but more subtle techniques are needed. For instance, if cortisone is administered to mice before tumour cells are injected into the tail vein, the mice die from hepatic rather than pulmonary metastases.[22]

The study of tumour-cell spread deserves more attention. Morphological and anatomical studies must be supplemented with physiological studies. The mechanisms of the dissociation of cancer cells, cell adherence, cell-to-cell compatibility, tissue pressures, and cell motility must be determined. We must learn more about the adhesion of tumour cells to blood-vessel walls, the role of fibrin in protecting the cells from toxic substances, and the manner in which tumour cells penetrate into the tissues.

CHEMOTHERAPEUTIC AGENTS

The practical application of information concerning the spread of tumour cells is being expanded as new chemotherapeutic agents are discovered. The Cancer Chemotherapy National Service Center is testing over 40,000 compounds each year for anticancer activity. The leukemias and lymphomas can be better treated with some of the new drugs, but most of them have been ineffective against the solid tumours. Nevertheless, there has been progress in the effective treatment of malignant chorioepitheliomas (a special situation) and cancers of the ovary and breast, and in the provision of systemic adjunctive therapy to surgical excision and irradiation.

SUMMARY

Tumour cells disseminate through lymphatics, blood vessels, and organ lumina, and exfoliate into the body cavities.

Tumour cells can be isolated from the veins draining the primary tumour. Such cells are also found in the peripheral blood of patients with advanced malignancy, and sometimes in the blood of patients with small, curable lesions. The frequency with which tumour cells are found in the blood parallels histological observations of blood-vessel invasion by the same kinds of malignancy.

Experimental models of clinical observations are useful but are not directly pertinent to human malignancy. Nevertheless, more observations should be made in regard to the mechanisms by which metastases are established.

The study of tumour-cell dissemination is particularly worthy of attention because of the great number of chemotherapeutic agents being investigated. Some carcinostatic agents, even though systemically ineffective against solid tumours, will probably be clinically useful against unestablished tumour cells.

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EMERGENCY TREATMENT OF COMMON TRAFFIC ACCIDENTS*

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To DEAL fully with a subject of this magnitude would require an extensive course in the pathology and surgery of trauma. In this short paper it is only possible to point out some important general principles around which more detailed knowledge may conveniently be arranged.

This report will deal briefly with principles of First Aid at the scene of an accident, and at greater length with the early stages of hospital care.

FIRST AID FOR TRAFFIC INJURIES

Before the doctor arrives, worthwhile help can be given by intelligent bystanders who have had training in the fundamentals of First Aid.‡ Certainly all traffic police and ambulance personnel should be so trained and should carry a few essential supplies such as large prepared dressings (e.g. "shell dressings"), bandages, wooden splints, and slings. They should understand and apply the following simple rules of First Aid:

1. Seriously injured casualties must be moved cautiously, avoiding unnecessary bending or twisting. They should be placed flat on a stretcher and not moved again. They should sit up only if able to do so without assistance.
2. All unconscious casualties should be placed in the prone or semi-prone position.
3. Wounds should be covered and kept covered with a sterile dressing held in place by a firm bandage. Bleeding should be controlled by direct pressure of the bandage, supplemented where necessary by hand pressure over the dressing.

   The tourniquet should NOT be used.

   Antiseptics should NOT be used on any wound.
4. When major fractures of the arms or legs are discovered, simple splinting should be applied *before* the patient is evacuated, e.g. the upper arm fastened to the body; the forearm splinted with a magazine or newspaper; a fractured femur dealt with by using the other leg as a splint or by using a long wooden slat on the lateral side of the leg; a fractured tibia or ankle managed by "the pillow splint".

It is a mistake to confuse non-medical personnel by complicated and impractical First Aid teaching, e.g. the types of hemorrhage, the use of pressure points, shock and its management, methods of splinting minor fractures, and classification of "insensibility".

When a doctor arrives at the accident scene he must ensure that each casualty has an adequate airway, that gross bleeding is controlled, and major fractures adequately splinted. Morphine is, of course, his greatest boon, but he should not give it indiscriminately—never to head-injury cases, and in only small amounts to those with extensive chest injuries leading to painful and difficult respiration.

Probably the most important duty of the doctor is to decide on the proper line of evacuation according to the number of casualties and the nature of their injuries. It is not always wise to send all casualties to the nearest "local" hospital. With certain types of serious lesions such as craniocerebral injuries, spine fractures, extensive maxillofacial fractures or wounds, "unstable" chest injuries, and compound fractures of the major bones, it may be wiser, after ensuring that First Aid measures are adequate, to send the casualties directly to the appropriate major hospital centre where a variety of special surgical services will be available.

EARLY HOSPITAL CARE OF TRAFFIC ACCIDENT CASES

Primary Assessment of the Injured Person

Of first priority is immediate recognition upon arrival at hospital of the very seriously injured patient whose resuscitation must be started at once. This is the casualty who is losing or has obviously lost a large amount of blood; he is pale, cold, clammy, and has a systolic blood pressure below 90 mm. Hg. He must be transfused immediately and at a rapid rate; further examination must be postponed until his blood replacement is well under way and his vital signs are improving.

All other casualties, less desperately ill than these, are well served by a rapid but careful and complete examination, amplified by such further information as may be obtained from a history of the accident and of the victim's behaviour since that time. All clothing must be removed and each area of the body systematically checked over. It should always be assumed that the injuries are multiple.

Wounds should be examined only while wearing a surgical mask. Hands should be scrubbed or gloved so that dressings may be gently lifted off and replaced; at this stage it is very wrong to "poke around" in wounds, as fresh massive bleeding may easily be stirred up. Bleeding which is not already controlled should, if possible, be managed by pressure dressings; a tourniquet should be employed only if amputation appears unavoidable; hemostatic forceps should be applied only to clearly visible bleeding points—to plunge them blindly into the wound may cause irretrievable damage to large vessels or nerves.

Almost all major fractures are easily detected by physical examination alone. Roentgenological examination is seldom urgent and is unlikely to add anything important to the primary assessment of the clinical problem. Moreover, it is dangerous to side-track badly injured patients to the radiology

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‡See St. John Ambulance manual, "Fundamentals of First Aid", published by the Priory of Canada, 1955.

department when they should be receiving urgent treatment for hemorrhage, respiratory difficulty, or unconsciousness. Skull films particularly are ill-advised at this early stage; they are time-consuming, necessitate potentially dangerous movement of an unconscious or comatose patient, and add little to one's knowledge of the nature and extent of intracranial damage. It is true that all fractures must ultimately be verified by x-ray, but this examination should be postponed until shock and hemorrhage are controlled, sedation administered, temporary splints applied, and brain, chest, or abdominal injuries carefully assessed and their management organized.

The Problem of "Shock" in Injured Casualties

The word "shock" should probably be dropped from medical terminology because it no longer has any precise meaning. It has instead come to be associated with a whole series of clinical states which have in common only certain superficial manifestations such as pallor, sweating, prostration, falling blood pressure, and tachycardia. Such a picture may result from many causes, such as hemorrhage, burns, severe diarrhea or vomiting, cardiac infarction, spinal cord injury, pulmonary embolism, peritonitis, bowel obstruction and vasovagal attacks. In each of these instances a quite different physiological mechanism is responsible for the clinical picture of "shock". Casual and uncritical use of the word "shock" under such varied circumstances diverts attention from the need for careful analysis of the causative factors. Only by clear appreciation of these underlying physiological disturbances can effective therapy be prescribed.

In relation to trauma, the condition to which the word "shock" has usually been applied can almost be equated with oligemia and this with hemorrhage, either external or hidden. Thus, instead of fruitless discussion as to whether the injured person is "in shock" or "not in shock", attention should be focused on making an intelligent appraisal of the amount of blood which has been or is being lost. In most of the seriously injured, this is the critical factor and the one which needs most urgent attention. Other factors, such as chest, cardiac, or cerebrospinal injury, may also contribute to the patient's total illness. These should be given separate careful consideration, for they may further reduce the patient's ability to maintain an adequate circulation of oxygenated blood.

In determining the amount of blood which an injured person has lost, pulse and blood pressure are of very limited value. These parameters bear no direct relationship to the degree of oligemia; they indicate merely the state of the patient's reaction to his injuries at that moment. For example, it is obvious that the casualty whose systolic pressure is below 70 mm. Hg, with a pulse of 120 per minute or more, and who is cold, pale and sweating, has lost a lot of blood; indeed it is probable that he has bled 40 to 50% of his total blood volume (2000 to 3000 c.c. in an adult) and that he will require rapid transfusion of considerably more than that amount to restore his circulation to a near normal state. On the other hand, it must be appreciated that a loss of 30 to 35% of a patient's total blood volume (1500 to 2100 c.c.) need not necessarily be associated with any apparent clinical disturbance of circulation; the patient may be pink, warm, and have a normal pulse and blood pressure. This same patient, apparently "not in shock", may quite suddenly exhibit profound collapse if he is carelessly moved, or if fresh bleeding is stirred up by manipulation of wounds or fractures, or if anesthesia is induced. Further, it is well known that in some patients who have lost 10 to 20% of their blood volume (500 to 1200 c.c.) the blood pressure may actually be elevated above normal level! Single measurements of pulse and blood pressure are thus of limited value; when, however, serial determinations are recorded over a period of time they may be helpful in indicating a trend towards recovery or deterioration.

The clinical assessment of blood loss in an injured person requires an intelligent guess based on a careful scrutiny of the nature and extent of the injuries, the presence or history of external bleeding, the amount of swelling of injured limbs, and the general reaction of the patient including the state of his pulse and blood pressure. With increasing experience one's "guesstimate" becomes more and more generous; actually it is very rare to overestimate the blood volume deficit. Multiple injuries usually mean a large blood loss; even small wounds of hands, face and scalp often bleed copiously. Practically all the swelling of a fractured limb is accounted for by hemorrhage, e.g. a closed fracture of the tibia with only moderate swelling of the leg may be accompanied by a blood volume deficit of 500 to 1100 c.c.; a fracture of the shaft of the femur regularly results in a loss of 500 to 2000 c.c. into the adjacent soft tissues, while those with extensive displacement of the fragments and much soft tissue damage may have even larger amounts of bleeding. Multiple fractures of the ribs can easily cause the loss of 1000 to 1500 c.c. of blood. With such yardsticks, based on actual blood volume measurements, one can make a reasonably accurate appraisal of the blood volume deficit in any given case.

The greatest single advance in the management of trauma has been the recognition of the extent and significance of blood loss and the importance of its rapid replacement by transfusion of whole blood. The common and tragic mistakes in the treatment of the seriously injured are:

1. Delay in starting transfusion (because the patient is "not in shock"!).
2. Blood dripped in too slowly (125 to 150 c.c. per hour, like a "routine" intravenous infusion).
3. Insufficient amount of blood transfused.

In all patients who have an estimated blood loss of 1000 to 1500 c.c. or more, transfusion must be started promptly. As a general rule, the worse the patient's clinical state, the greater the evidence of blood loss, and the shorter the time since injury, the more urgent it is to start blood replacement and the more quickly it should be administered. Large needles or cannulae, or plastic tubing should be introduced, preferably in at least two veins, so that blood or blood substitute may be given at a rapid rate. It is probably best to start the infusion with 5% glucose in water. Then if the patient's condition is really serious it will be necessary to follow quickly with either Group O (preferably Rh-negative) blood, or a plasma expander (e.g. dextran), but, as a general rule, not more than one litre of the latter should be given since it has no oxygen-carrying capacity. Within 30 to 45 minutes cross-matched blood should be available and this should be given rapidly, e.g. 500 c.c. every four to ten minutes, until it is estimated that the deficit has been replaced, then more slowly to keep up with the bleeding which may continue for a day or more into the injured tissues.

When the initial blood loss has been massive, it is often true that adequate blood transfusion will stimulate further bleeding, so that it may be necessary to replace the entire blood volume several times in the course of a few hours. This requires boldness, skill, and good organization; it is not always successful but in desperate cases the alternative is certain death. Experience in the Korean War demonstrated repeatedly the effectiveness of massive rapid transfusion in saving the lives of young men gravely injured.

It may be difficult to judge when blood replacement has been adequate. If in doubt, it is best to err on the side of giving too much rather than too little. The return of a pink warm condition to the skin is an encouraging sign; attainment of normal blood pressure and slowing of the pulse are confirmatory evidence of effective therapy. Failure to respond to rapid transfusion means unrecognized injury usually needing urgent surgical intervention.

The overriding importance of giving whole blood quickly for the resuscitation of the badly injured casualty has been deliberately stressed. Ancillary methods are of negligible value. Oxygen is useless, except as a supplementary measure in dealing with those who have mechanical interference with respiration. Heat is definitely harmful; it causes only vasodilatation of the skin and sweating; the patient suffering from major blood loss should be kept cool. Noradrenaline or other vasopressor drugs are rarely, if ever, indicated in the presence of oligemia; they increase the work of the heart and, by causing prolonged renal ischemia, greatly exacerbate the danger of renal failure. Corticosteroids are of no value in acute trauma, except in the rare instance of a patient who has recently been receiving such therapy; under such circumstances large doses of the intravenous hormone are required.

The Early Treatment of Wounds

Primary healing of wounds will be obtained in most instances if clean viable tissues are approximated without tension; this is the objective of wound toilet (debridement). Chemical antiseptics have no role whatever in the treatment of wounds; the best antiseptic is the scalpel. Antibiotics are of limited value; in most cases they are unnecessary; they are definitely indicated only in dealing with grossly contaminated wounds, or in those which are already "inflamed" by delay in surgical treatment.

It is wrong to give 1500 units of antitetanus serum routinely to every person with a cut or laceration. The risk of anaphylaxis or urticaria or serum sickness far outweighs that of developing tetanus in wounds which are properly cleaned and debrided. Persons previously immunized should receive a "booster" dose of tetanus toxoid while all others should be given an initial dose of toxoid and arrangements made for them to complete a course of active immunization. A.T.S. should be reserved for those whose wounds are considered especially liable to tetanus infection, e.g. puncture or stab wounds, or those contaminated with street or farm dirt. In these instances, after suitable testing, 5000-10,000 units of A.T.S. should be given in addition to toxoid (and in a separate syringe!). Penicillin and tetracycline should also be prescribed in these cases and the wounds left open.

Except for minor lacerations, wound toilet should always be carried out under aseptic conditions in a proper operating theatre. General anesthesia is frequently required; a tourniquet is of value in dealing with wounds of the extremities. Soap and water or a detergent are applied vigorously (with a brush if necessary) to cleanse a wide area of surrounding skin, which is then shaven and rinsed with large amounts of sterile saline. The wound is opened, washed out with saline, and inspected both visually and with the exploring finger. When damage to underlying tissues appears extensive it is important to extend the skin wound for adequate exposure. Incisions for this purpose should be carefully planned; running along natural skin creases wherever possible, otherwise in a sinuous manner so as to avoid long straight scars. Such incisions should never run longitudinally across the front or back of a joint. Further exploration and irrigation of the wound is now possible and foreign bodies are removed. Excision of devitalized muscle or fat should be generous, excision of skin edges should be minimal, and, in many cases, particularly on the hands or face, it should be avoided entirely. Tension in muscular compartments must be relieved by extensive cruciate incisions of the deep fascia. Finally, further irrigation with large amounts of sterile saline serves to remove the last vestiges of blood or blood clot, foreign material or loosened tissue fragments.

Primary closure should be possible in most cases even up to 24 hours after injury if the wounds are

not thought to be heavily contaminated and are not associated with extensive bruising and crushing of the tissues. When in doubt, however, it is always safe to leave the wound open, not packed tightly, but with wound surfaces separated by a strip of Vaseline-impregnated gauze; delayed primary closure in two to 10 days will generally be possible.

Suturing of debrided wounds is preferably confined to skin only; deep sutures are employed only when necessary to obliterate dead space. If drainage is thought necessary, primary closure should NOT be attempted. When skin deficit makes closure difficult, those with experience will not hesitate to employ local tissue shift or dermatome grafts.

Careful pressure dressings are helpful in minimizing oozing and giving relief from pain. A light plaster cast over the dressing is often advisable to give the added advantage of immobility and to discourage meddlesome "peeking" at the wound.

The Early Treatment of Fractures

Reference has already been made to the importance of early splinting of major fractures, and to the absolute priority of blood volume replacement over the definitive treatment of any specific injuries.

The main decision with regard to a broken bone is whether or not to perform open reduction. In major centres under ideal peacetime conditions the trend is definitely towards operative reduction and internal fixation of the majority of difficult fractures. It must not, however, be forgotten that such procedures always entail serious hazards such as infection leading to osteomyelitis, devitalization of bone fragments by separating them from soft tissue attachments, and delayed union or nonunion from the above factors or from faulty application of metallic fixation. Specific mention should be made of the risks of so-called "external skeletal fixation". The idea of drilling steel pins into broken bones at a distance from the fracture site and connecting them by bars and bolts to maintain reduction sounds simple. In truth it is a method which is fraught with danger unless the operator has particular skill and experience. Skin necrosis, pin-track infection, osteomyelitis, joint infection and fixation of ligaments and tendons will result from the slightest errors of technique. It is a method NOT recommended for general use.

Unless one has the advantage of training and experience in the techniques of fracture surgery plus adequate operating facilities such as a variety of special instruments, screws, nails, plates and pins, as well as radiographic control, it may be disastrous to attempt operative fixation of fractures. But there can be no criticism of an attempt to do the best possible by conservative methods such as closed reduction or skin traction; consultation and, if necessary, referral to a special centre can always be subsequently arranged.

With compound fractures the major consideration is to obtain primary wound healing without infection. Wound toilet should be meticulous. Fractured bone surfaces must be carefully cleaned; embedded dirt can be removed with a curette. Only tiny bone fragments free from all soft tissue attachments may be sacrificed. If the fracture can be stabilized easily by one or two stainless steel screwnails or by a small plate, one should not hesitate to do so. When, however, internal fixation appears difficult, it is probably wiser and safer to deal only with the wound, irrigating and debriding and suturing it in the hope of getting primary closure. The fracture can be immobilized by simple means and, if necessary, dealt with by re-operation within a few weeks.

Chest Injuries

When dealing with injured persons never treat dyspnea with morphine; analyze the mechanism of dyspnea and deal with it by some more rational method.

Broken ribs are painful, so that breathing and coughing are always interfered with to some extent; the pain can best be relieved by intercostal nerve block using local anesthesia.

Dyspnea will probably be exacerbated whenever rib fractures are associated with bleeding into the pleural cavity, i.e. hemothorax, or with laceration of the lung leading to pneumothorax. One should always look carefully for such complications, using physical and, if necessary, roentgenological examination. Whenever there is the slightest doubt, exploratory aspiration of the pleural space should be carried out, tapping both front and back of the chest on each side. Either air or blood should be evacuated as completely as possible and as frequently as necessary, so that expansion of the lung may be maintained. Very occasionally a laceration of the lung acts like a flap valve so that with each expiratory effort more air is forced into the pleural space. This rapidly builds up a positive-pressure pneumothorax which is very dangerous—one of the real emergencies of surgical practice. The patient becomes very distressed and extremely dyspneic; tachycardia, neck vein distension, and lateral displacement of heart or trachea may be detected as well as hyperresonance and absent breath sounds over the involved hemithorax. A large bore needle must be quickly plunged into the pleural space between the upper anterior ribs; air will escape under pressure; the needle may be fixed in position by adhesive tape and connected to an underwater drain. The relief afforded by this simple measure is one of the most dramatic incidents in surgical practice; the penalty for failure to make the diagnosis and deal with it quickly is a dead patient.

The stove-in chest or "steering wheel chest" is a dreadful injury which has been responsible for many deaths from traffic injury. A large segment of the chest wall often including the sternum is

floating free of lateral and posterior attachments. This segment will be seen to move inwards on inspiration and outwards on expiration, so-called "paradoxical respiration". Air exchange is seriously hampered; carbon dioxide retention and oxygen deficit develop rapidly. Coughing is impossible because of pain, so that bronchial secretions, increased in amount under these circumstances, cannot be evacuated; obstruction of bronchioles and smaller bronchi leads to progressive atelectasis, causing further interference with gaseous exchange. At the same time disturbances of the intrathoracic pressure relationships inhibit venous return and reduce cardiac output.

Only in recent years has it become possible to save the lives of any significant number of persons with this injury. Partial stabilization of the floating segment of the rib cage so as to diminish its paradoxical motion may be accomplished by the use of sandbags or by pressure strapping over large dressing pads. In cases of minor instability this may serve as definitive treatment. For more serious instances such measures can give only temporary and imperfect relief.

The employment of tracheostomy in these major chest injuries has been a great advance. It makes breathing easier and more effective by reducing the dead space in the upper air passage; it enables bronchial secretions to be cleared by frequent aspiration. It should be done early before the patient is critically ill from anoxia. This is a procedure which every doctor must be prepared to do quickly and well if there is any possibility that he may be responsible for the early care of accident victims. It may be accomplished under local anesthesia but it is much easier, whenever possible, to do it quietly with the help of general anesthesia maintained by intratracheal intubation.

A relatively recent but equally dramatic advance in the handling of these difficult problems has been the use of controlled positive-pressure respiration. A special cuffed tracheostomy tube (e.g. the "James tube") is introduced and connected to an automatic machine which rhythmically inflates and empties the lungs. Paradoxical movement of the chest wall is at once controlled; dyspnea is almost eliminated; pain is reduced; oxygenation is restored; fear is relieved. The principle is simple, its practical application full of complexities. Physicians and nurses with special knowledge and training are required to be in almost constant attendance. Centralization of apparatus and talent is mandatory. In the Toronto General Hospital this has led to the setting up of a "Respiratory Unit", to which all patients who need this type of expert care may be admitted. I believe that such units should be established at other centres throughout the country; no patient with serious chest injury should be denied this lifesaving help.

SUMMARY AND CONCLUSIONS

In this short presentation an attempt has been made to emphasize some important general principles in the care of traffic accident casualties. Stress has been laid upon the importance of simple First Aid measures at the scene of an accident and of the doctor's role in deciding on the proper line of evacuation. The early assessment of the injured person has been discussed, emphasizing that roentgenological examination should usually be postponed until other more urgent measures have been carried out. An attempt has been made to divert attention from the problem of "shock" and to focus it instead upon the question of the amount of blood loss and the importance of replacing it quickly by transfusion of whole blood. Reference has been made to the negligible value of ancillary methods of resuscitation such as the use of oxygen and vasopressor drugs. In relation to wounds, attention has been directed to the importance of surgical "wound toilet", while the role of chemical antiseptics and of antibiotics has been played down. As far as fractures are concerned, the hazards of internal fixation when performed under other than ideal circumstances have been stressed. In regard to chest injuries caution has been urged in the use of large doses of morphine, and, instead, a plea has been made for analysis of the exact nature of the injury and its complications. The principles of rational therapy of chest injuries have been indicated briefly and special attention has been drawn to the value of the "Respiratory Unit" in the care of those casualties with multiple rib fractures leading to paradoxical respiration. No reference has been made to many other types of injury which may result from traffic accidents, e.g. blunt trauma to the abdomen, head injury, maxillofacial injuries, vascular injuries and hand injuries. The principles that have been outlined are generally applicable to these special instances; their detailed care may, however, involve complexities far beyond the scope of this presentation.

PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

The ninth regular meeting of the British Medical Association, Halifax and Nova Scotia branch, was held in the City Hall, Halifax, on February 13. Dr. John Stewart read a paper on "Some Points in the Pathology of Tuberculosis and in the Treatment of Surgical Cases". Dr. Stewart considered the subject under the headings of Paths of Infection and Treatment, pointing out, in the former, the increasing appreciation of the importance of the alimentary tract as a portal of infection, especially in children; and in the latter, dealing chiefly with some of the recognized methods in surgical treatment—the vaccine treatment, by tuberculins; in osseous affections, counter-irritation; the Bier method, and a combination of this with the local use of iodoform, as employed by Mikulicz; in tubercular abscesses, aspiration followed by the injection of iodoform; and in tuberculosis of the cervical glands, tuberculin, before having recourse to operation.—*Canadian Medical Association Journal*, 1: 481, May 1911.

AN OBJECTIVE ASSESSMENT OF THE EFFECTS OF NIALAMIDE ON DEPRESSED PATIENTS*

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SOME OF THE NECESSARY characteristics of adequate studies of the effects of drugs used in psychiatry have been summarized by Marley.[1] Among such criteria are the following.

(a) *Selection of patients.*—It is desirable, in any attempt to assay the effects of treatment, to ensure that the patients involved in the trials should constitute as homogeneous a group as possible. If this precaution is neglected, any positive effects of the drug on one kind of patient may be swamped by its lack of effect on others, or even cancelled out by its negative effects on some.

It is, of course, recognized that the basis of such homogeneity may be very difficult to specify in the case of psychiatric patients, since even single diagnostic categories can be shown to comprise a large degree of heterogeneity. However, in many of the published studies on the effects of nialamide, little attempt has been made to secure even such homogeneity as may be derived from the use of psychiatric diagnostic labels. A study of the effectiveness of nialamide in the treatment of depression by Vaisberg *et al.*,[2] for example, included some patients diagnosed as suffering from manic-depressive psychosis, involutional psychosis, psychoneurosis, psychosis with cerebral arteriosclerosis and psychosis with mental deficiency. It was claimed that these patients were chosen because they all showed symptoms of profound and persistent depression and anergy. It is unlikely, however, that with such divergent diagnoses, their symptoms were of very striking similarity. That the drug proved effective in no fewer than 16 out of 26 patients (i.e. in about 60% of the cases used) is probably due more to the self-limiting and episodic nature of many psychiatric illnesses than to the methodology of the trial or the efficacy of the compound.

(b) *Experimental controls.*—It would seem trite to emphasize the need, in drug studies, for the control of those factors which may cause apparent changes in outcome but which are, nevertheless, unrelated to any specific drug action. It must be remembered, for example, that the natural history of depressive illnesses tends towards spontaneous recovery and it is only against the yardstick of this kind of change that the efficacy of any new remedy may be assessed.

Among the other possible sources of variation, one which, if not well understood, is at least well recognized, is the so-called "placebo reaction". Trouton[3] has pointed out that the less certainty there is about the effect of a given drug the more important is information about placebo reaction in the assessment of its effects. Of those reports which have tried to estimate the action of nialamide few have acceded to the requirements of scientific method so far as to provide for checks on this kind of reaction.

Hollister *et al.*,[4] in their study, it is true, switched 7 out of 20 patients to doses of an inert substance at the end of the clinical trial. This concession, however, does not conform even to the most lenient standards of experimental design.

Although critics like Tuteur[5] have made objections to the so-called "double-blind" method, its possible inadequacies provide no excuse for the neglect of the most elementary experimental precautions.

(c) *Assessment of effects.*—It is notorious that one of the most refractory problems in psychiatric research is that of the assessment of clinical improvement. Descriptions of behaviour abnormalities are usually themselves so imprecise that the detection of quite gross changes, and, of course, still more the exact measurement of minor alterations, are matters of great difficulty. This is another reason for advocating the kind of constraints imposed upon clinical judgment by the double-blind method of investigation. Even when this technique is impracticable, the use of objective, systematic tests may provide an invaluable check upon judgments and impressions.

One of the few attempts that have been made to objectify observations in the case of subjects treated with nialamide is the study by Alexander and Lipsett[6] assessing its relation to change in the conditioned psychogalvanic reflex in psychiatric patients. Although these authors claim that effective dosage may be associated with the diminution of such response, the well-known unreliability of measures of this reflex and the lack of any control group certainly vitiate their conclusions.

In the light of such criticisms of previous work with this drug, a study was designed to try systematically to assess some of the changes in functions which might be expected to accompany improvement if nialamide were indeed successful in the alleviation of depression.

METHOD

Subjects.—Two groups of 13 patients were examined, comprising the majority of individuals with a diagnosis of depression admitted to the Kingston General Hospital during the period of this study. Only patients who were overtly suicidal or too agitated to be tested were excluded. Each patient was randomly assigned to one group or the other. The first group was treated with nialamide and consisted of 7 men and 6 women with an age range from 21 to 64 years. Of these, 9 were diagnosed as suffering from manic-depressive reaction, depressed type, 4 as psychoneurotic de-

*C. Pfizer and Co. Ltd. kindly supplied generous amounts of nialamide (Niamid) and other compounds used in this experiment.
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pressive reaction. The other group was treated with an inert preparation; there were 8 men and 5 women in this group whose ages ranged from 17 to 63 years. In this group there were 2 patients diagnosed as manic-depressive reaction, depressed type, and 11 suffering from psychoneurotic depressive reaction. The unfortunate differential bias in diagnostic categories was undoubtedly a function of the difficulty of randomizing small samples. A more equitable distribution of diagnoses would no doubt have been obtained if the experiment had been extended and larger numbers accrued. In all these patients, however, the severity of the depression was sufficient to have demanded hospital admission and, in the pre-drug era, electroconvulsive therapy.

The double-blind procedure was used and only the hospital pharmacist knew which treatment each patient was receiving in 50-mg. doses thrice daily.

Each patient was assessed twice on eight tests. The first testing was done as soon as the patient came into hospital and before any treatment had been given. The second testing session was carried out after a minimum of 14 days and usually after about 21 days of treatment. There was no difference in length of treatment between the two groups.

Weekly serial liver function tests (serum bilirubin, alkaline phosphatase, transaminase and thymol turbidity), full blood counts and urine examinations were performed without untoward results. Four-hourly blood pressure and pulse estimations throughout the day failed to reveal any hypotension.

Tests.—The tests were chosen for their apparent ability to assess some of those aspects of the patients' behaviour which could be expected to vary with depressive illness and recovery. They were always given in the same order.

One advantage, among others, which objective tests have over clinical impressions as measures of drug action is the possibility that exists of using them as both criterion and as predictor variables. Thus, if the drug were to prove to be more effective than placebo treatment, changes in the test results might provide a dependable index of improvement. In addition, the initial test results might be associated with different degrees of improvement within the treated group. Even if the treatment should, on the other hand, prove to be unsuccessful, the first test results might still be associated with different degrees of spontaneous change within the groups with time. Such a useful double function cannot be expected of the indices of change which involve only psychiatric opinion about outcome *after* treatment.

The items used in this study with these expectations comprised tests of personality and mood, cognitive level and speed, psychomotor functioning and impressions of sickness, as follows.

1. PERSONALITY AND MOOD

(a) *The Maudsley personality inventory.*—This is a personality questionnaire developed by Eysenck[7] which purports to give estimates of the personality variables introversion-extraversion and neuroticism. There is evidence that some depressive patients are both introverted and neurotic.[8] It is conceivable that the depressive illness itself may have some influence upon the measures used to estimate these variables.

(b) *The Hildreth feeling scale.*—This is a test devised by Hildreth[9] which is intended to give an estimate of the subject's experience of depression or elation.

2. COGNITIVE LEVEL AND SPEED

(a) *The Nufferno level test.*—This is a cognitive test devised by Furneaux[10] which consists of items of ascending difficulty made up of series of letters followed by a dot. The subject's task is to discover the principle involved in each series and to supply the missing letter. Thus, in the series AABBCCD the missing letter would be D. Ample time is allowed the subject, who is instructed to work at his own speed. The score is derived from the number of items correctly completed.

There is some evidence that depressive illness may affect general intellectual level, so that changes even in this characteristic might occur with clinical alterations in psychiatric status.[11]

(b) *The Nufferno speed test.*—This cognitive test consists of a series of items[12] similar to those in the Level Test but of a very much simpler nature, such that most subjects find them well within their ability. The score on this test is derived from the speed at which the subject solves those items he completes correctly.

There is a good deal of evidence that some patients diagnosed as depressives are abnormally slow on this kind of mental test.[11]

3. PSYCHOMOTOR FUNCTIONING

(a) *Speed of tapping test.*—This is an unstandardized, but commonly used, psychomotor test. The subject is simply required to tap as fast as possible for three 10-second trials on a Morse key. Two scores were obtained. One was simply the sum of the number of taps recorded in each trial; the other was the sum of the number of taps recorded on each occasion after the instructions to stop tapping had been given. The latter score was taken as an indication of "perseveration".

There is evidence that rate of tapping is slowed down by disorders such as depression.[13]

(b) *Manual and finger dexterity.*—The psychomotor tests of the United States Employment Service[14] General Aptitude Test Battery were used. The Manual Dexterity test requires the subject to place and turn pegs in a peg-board and involves large hand and arm movements. The Finger Dex-

TABLE I.—MEANS, STANDARD DEVIATIONS AND THE SIGNIFICANCE OF DIFFERENCES IN CHANGES BETWEEN TEST AND RETEST IN THE DRUG AND PLACEBO CRITERION GROUPS

	Experimental Group (N = 13)				*Control Group (N = 13)*					
	Test		*Retest*		*Test*		*Retest*		*t*	*p*
	$\bar{m}$	σ	$\bar{m}$	σ	$\bar{m}$	σ	$\bar{m}$	σ		
Age	44.85	11.65	—	—	41.85	13.30	—	—	0.612*	NS
M.P.I.										
Extraversion	18.62	11.18	20.77	12.99	26.92	7.88	24.77	10.09	2.025	<.025
Neuroticism	26.92	12.17	26.77	13.37	26.46	8.42	25.38	12.27	0.481	>.30
Hildreth Scale										
Feeling	3.98	1.11	3.92	1.28	4.02	1.71	4.33	1.89	0.505	>.30
Attitude	5.65	1.05	5.50	1.43	5.66	1.16	5.68	1.66	0.145	NS
Average	4.81	0.88	4.71	1.24	4.84	1.32	5.00	1.62	0.576	>.25
Nufferno										
Level	255.42	153.65	259.33	170.05	213.58	116.86	241.33	164.44	0.786	<.20
Speed	171.00	54.96	187.67	18.06	170.83	58.16	170.00	53.36	0.638	>.25
Tapping										
Speed	159.31	43.18	160.85	50.10	181.15	41.12	182.31	40.99	0.036	NS
Perseveration	5.15	1.12	4.23	1.31	5.15	2.39	6.31	2.29	3.049	<.005
USES Dexterity										
Manual	43.08	34.88	48.85	45.82	42.08	29.42	54.77	43.82	0.608	>.30
Finger	62.62	25.11	59.15	25.15	59.77	23.18	65.15	31.94	0.284	NS
Printing Speed	7.75	2.72	8.50	3.43	6.83	2.00	7.92	2.77	0.185	NS
Depression Rtg.										
Psychol.	12.77	2.07	12.00	3.17	14.42	2.37	14.00	3.44	0.270	NS
Psychiat.	12.70	2.36	10.50	2.59	13.58	3.82	11.17	5.33	0.229	NS

*2 tail test of significance.

terity Test requires the subject to assemble and disassemble small washers and rivets and place them in a peg-board; it involves mainly fine finger movements.

Yates[13] has noted that relatively little work has been done on the use of these tests with abnormal groups. Since they ostensibly involve both motor speed and accuracy, however, they seem to be related to abilities that may change with alterations in depressed states.

(c) *Speed of printing.*—This is an unstandardized test. The subject is simply told to print the letters of the alphabet as fast as he can. The score is the number of letters printed in one 9-second trial.

4. IMPRESSIONS OF SICKNESS

(a) *Depression rating scale.*—This is a scale specially devised for this study which divides the symptomatology of depression into such components as mood, retardation, appearance and agitation. It also provides simple descriptive illustrations of these aspects in terms of varying severity so that they may be systematically rated on a five-point scale. Each subject was rated on these aspects of his behaviour at the beginning and at the end of the treatment period by both the psychologist, who carried out all the other tests, and by the psychiatric resident in charge of the case.

(b) *Psychiatric opinion.*—A simple "improved-unimproved" rating was also made of each patient at the end of the trial by the attending staff psychiatrist. His judgment was made as independently as possible from that of the psychiatric resident, although in every case both had seen and discussed the patient.

If the patient were sufficiently well to be discharged home without any further treatment, and remained out of hospital for at least three months, he was judged "improved". Although retesting usually took place at the end of three weeks, the patients were not always discharged immediately, even in the "improved" cases, although the latter usually left hospital within a week or two. The patients who were judged "unimproved" at the end of the drug trial were then given from 8 to 10 electroconvulsive treatments over the next month. All these "unimproved" patients except one (a patient with predominating hypochondriasis) eventually "improved" on this regimen, according to the criteria defined above.

RESULTS

Differences between groups.—The significance of the differences on all the test variables, between the criterion groups, was assessed by the uncorrelated one-tailed t-test.[15] The results obtained are shown in Table I.

There is a striking overall lack of any consistent or systematic change with treatment. Not all the changes even went in the expected direction. The reverse was true for the Hildreth Feeling Scale and the Finger Dexterity Test.

Since so many differences have been examined, the fact that 2 out of 14 do show a significant change in the expected direction must be interpreted with caution.

The apparent increase in extraversion on the part of the experimental group is, however, of interest. Eysenck[16] has developed a theory of drug action in relation to personality variables which states that depressant drugs increase cortical inhibition, decrease cortical excitation and thereby produce extraverted behaviour patterns. The tentative interpretation of the present results would be that nialamide is functioning as a cortical depres-

TABLE II.—ASSOCIATION BETWEEN PHYSICIAN'S RATINGS AND GROUP MEMBERSHIP

	Treatment group	
	Experimental	*Control*
Rating		
Improved	4	6
Not improved	9	7
$X^2 = 0.650$	NS	

sant. This seems to be counter to the views of some investigators (e.g. Vaisberg *et al.*[2]) who refer to it as a "psychic stimulant", but more congruent with the findings of Rowe,[17] who showed that nialamide may potentiate the effects of hexobarbital, although to a lesser degree than iproniazid. It should be noted, however, that Caird, Sloane and Inglis[18] failed to find any potentiating effect of nialamide, in single acute doses of up to 150 mg. on alcohol, an undoubted cortical depressant. Sloane[19] has argued that psychological depression may so often be associated with physiological stimulation that the administration of a cortical depressant to counter behavioural depressions may not be so incongruous as it seems at first sight.

The second positive significant finding is that, on the single test of "perseveration" used, the experimental group improved more than did the control group. It is tempting to regard this as evidence for some reduction in retardation, an interpretation which, however, runs counter to the insignificant results obtained on the other mental and motor speed tests.

The results on the dichotomous scale used by the attending staff psychiatrist are shown in Table II. It can be seen from this that no significant differential change has taken place so far as clinical impression is concerned.

Test Results and the Prediction of Outcome

With regard to the possible usefulness of the various tests as predictors, rather than as criterion variables, the relation between results on these items, on the first occasion of testing, and outcome, as assessed by the estimate made by the attending psychiatrist, was measured by point biserial correlations.[15] The results are shown in Table III.

TABLE III.—POINT-BISERIAL CORRELATIONS BETWEEN PHYSICIAN'S RATING AND TEST VARIABLES WITHIN GROUPS

	Experimental		*Control*	
	rpb	*p.*	*rpb*	*p.*
M.P.I.				
Extraversion	.108	NS	−.083	NS
Neuroticism	−.052	NS	.079	NS
Hildreth Scale				
Feeling	.028	NS	−.276	NS
Attitude	−.194	NS	−.170	NS
Total	−.093	NS	−.126	NS
Nufferno				
Level	.092	NS	−.324	NS
Speed	.084	NS	.145	NS
Tapping				
Speed	−.096	NS	−.013	NS
Perseveration	−.062	NS	−.048	NS
USES Dexterity				
Manual	−.033	NS	−.215	NS
Finger	−.030	NS	−.035	NS
Printing Speed	−.006	NS	−.348	NS
Depression Rating				
Psychologist	.118	NS	.344	NS
Psychiatrist	−.026	NS	−.017	NS

It can be seen from this table that there is not a single item that is significantly correlated with differential outcome within either the experimental or the control group. It must be remarked, however, that this way of using the test data falls back upon clinical impression as the principal criterion variable, a procedure which, as noted above, has many disadvantages.

DISCUSSION

Neither way of using the objective psychological tests, as criteria or as predictors, produced encouraging results in relation to the effects of the drug as it was used in this study. This outcome perhaps epitomizes the dilemma of all drug studies. If we employ systematic, objective measures and secure positive results, we may then gain confidence in both treatment and estimates. If, on the other hand, no such results appear, it is difficult, if not impossible, to establish whether this is because the drug is quite ineffective, or only ineffective in the dosage used or over the length of the trial period, or if the tests employed have simply been insensitive or unrelated to actually induced alterations in function.

The present results do, however, indicate that nialamide in the dosage described over a treatment period of three weeks failed to improve patients who were subsequently successfully treated by electroconvulsive therapy (E.C.T.). It is most unlikely that this later improvement by a known remedy could have been initiated or facilitated by the preliminary three weeks of nialamide treatment, since there was a similar subsequent improvement, after E.C.T., shown by members of the placebo group. It must be admitted, however, that owing to the imbalance of depressive types within each group, the relative effect, or lack of effect, of nialamide on psychoneurotic depressive reaction as compared to manic-depressive reaction, depressed type, could only be elucidated by a further study.

There is at least one way of finding out whether the lack of alteration in the test results is due simply to the insensitivity of the test items. It depends, unfortunately, upon the subjective judgment of improvement as its main criterion.

In the present study, for example, it has been shown that there are no differences in test results or improvement rates between the criterion groups. Nevertheless, some individuals did apparently improve, according to the definition cited, over the trial period. The sensitivity of the items used might therefore be assessed by comparing differences in test and retest scores, not, as formerly, between the drug and placebo groups, but using the two groups comprised of those patients judged "improved" and those judged "unimproved". The results of such comparison are shown in Table IV.

TABLE IV.—MEANS, STANDARD DEVIATIONS AND THE SIGNIFICANCE OF DIFFERENCES IN CHANGES BETWEEN TEST AND RETEST IN THE IMPROVED AND UNIMPROVED GROUPS

	Improved Group (N = 10)				*Unimproved Group (N = 16)*					
	Test		*Retest*		*Test*		*Retest*		*t*	*p*
	$\bar{m}$	σ	$\bar{m}$	σ	$\bar{m}$	σ	$\bar{m}$	σ		
Age	39.70	14.75	—	—	45.62	10.44	—	—	1.201	<.20*
MPI										
Extraversion	23.80	10.47	23.20	11.16	22.12	11.18	22.50	12.91	0.417	NS
Neuroticism	29.00	7.53	28.00	14.05	25.25	11.29	24.88	12.80	0.031	NS
Hildreth Scale										
Feeling	4.17	1.72	5.09	1.43	3.89	1.33	3.53	1.55	1.819	<.05
Attitude	5.73	1.15	6.34	1.36	5.60	1.15	5.12	1.55	1.631	<.10
Average	4.94	1.32	5.71	1.15	4.75	1.05	4.32	1.44	1.875	<.05
Nufferno										
Level	240.44	182.20	281.11	195.10	230.93	131.88	231.87	159.29	1.297	<.15
Speed	199.11	68.53	173.11	65.81	154.00	67.34	182.27	18.64	2.077	<.025
Tapping										
Speed	165.20	13.82	175.20	37.14	177.12	43.18	172.44	17.26	1.390	<.10
Perseveration	5.10	2.38	5.80	1.75	5.19	1.60	4.94	2.22	1.186	<.15
USES Dexterity										
Manual	43.30	23.19	67.20	26.33	40.88	38.36	42.19	53.17	1.110	<.15
Finger	71.20	24.18	78.10	27.58	55.12	23.69	57.56	33.20	0.621	<.30
Printing Speed	7.22	2.17	9.22	2.54	7.33	2.71	7.60	3.48	1.538	<.10
Depression Rtg.										
Psychol.	13.90	2.85	11.60	1.65	13.33	2.19	13.87	4.16	1.574	<.10
Psychiat.	13.44	4.09	8.78	3.94	13.31	2.60	12.31	3.93	2.927	<.005

*2 tail test of significance.

From these data it can be seen that, while not all these changes are significant at the commonly accepted levels of confidence (0.05 or 0.01), there is, nevertheless, a much greater tendency towards significance than was shown in Table I.

In this case three of the differences are in the reverse of the expected direction; these are the changes in extraversion, mental speed and perseveration. These reversals are the more unexpected in that two of them occur on the very variables on which nialamide apparently had an effect, in the "expected" direction, in the case of the original criterion groups. If this comparison be taken at its face value, it would seem to suggest that the effect of nialamide is to alter certain aspects of function in a direction opposite to the changes that take place with improvement.

The majority of the findings summarized in Table IV are not to be explained in terms of any contamination effect, since the attending psychiatrist's "improved-unimproved" ratings were made without any knowledge of the actual test results. An exception to this rule is probably reflected in the highly significant difference in change in the Depression Rating Scale results as these were assessed by the psychiatric resident. Undoubtedly these figures are, in part, at least a function of the kind of indirect contamination that has been analyzed by Shapiro *et al.*[20] Thus, while the "improved-unimproved" ratings were made by the attending psychiatrist without any knowledge of the actual test or Depression Rating Scale results, he could not fail to found his judgment of such change on those very aspects of functioning which this rating scale was designed to objectify. At most, then, this result indicates that the rating scale and the psychiatrist's judgment were both related to much the same areas of behaviour.

SUMMARY

A study of the effects of nialamide on depressed patients, including both manic-depressive reaction, depressed type, and psychoneurotic depression, using objective tests both as criterion and as predictor variables, has been conducted. There were few significant test differences between a drug-treated and a placebo-treated group; nor was there any difference in the clinically assessed improvement rate between these groups. An attempt has also been made to see if the lack of change in test results was simply due to the insensitivity of the measures used. There is some evidence that this was not the case.

It was concluded that nialamide in a dosage of 50 mg. thrice daily for 21 days had no better an effect on depressive illness than a placebo medication.

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FURTHER OBSERVATIONS ON THE PSYCHOSOMATIC CHARACTER OF TOXEMIA OF PREGNANCY*

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THE MINNESOTA Multiphasic Personality Inventory (M.M.P.I.) has been used to implicate personality decompensation resulting from stress as the etiological mechanism in toxemia of pregnancy.[5] Further support for this theory is offered by the following case history.

A 27-year-old gravida 2, para 1, unmarried coloured female came to hospital at term in labour. She had had a Cesarean section to terminate her first pregnancy because of premature separation of the placenta. During the current pregnancy she had not sought prenatal care. Examination on admission revealed a blood pressure of 160/100 mm. Hg, 2+ albuminuria, and edema, with a total weight gain of 43 lb. While being prepared for repeat section, she impressed the attending team with her feelings of persecution and complaints that she was not receiving sufficient attention. At repeat section, a viable female infant in good condition weighing 2892 g. was delivered. Her blood pressure was 120/40 and pulse 72 immediately postoperatively. The feelings of persecution persisted after delivery and she inquired on several occasions when her baby would be delivered. At eight hours post-delivery she convulsed. Her blood pressure at this time was 200/70. No further convulsions occurred, but during the next 24 hours the blood pressure varied between 195 and 200 mm. Hg systolic and 70 and 105 diastolic. She continued to receive sedation and antihypertensive drugs. Urine output remained good. During this time she remained convinced that she was still pregnant despite repeated assurance to the contrary. She also continued to be paranoid in her thinking. About 30 hours post-delivery, she was finally convinced that delivery had taken place and thereafter all signs of toxemia quickly vanished. Her personality likewise appeared to change and she became very co-operative, humble and overly pleasant, to an artificial degree.

To explore further the role of the psyche in the genesis of toxemia of pregnancy, the M.M.P.I. test was given to 41 patients with this disorder. Thirteen of the 41 subjects received the M.M.P.I. test immediately post partum and 28 were given the test in the antepartum period. All were derived from a medically indigent population at Herman Kiefer Hospital. Thirty-two had pre-eclampsia, seven had hypertension with superimposed pre-eclampsia and two had eclampsia. Pre-eclampsia was defined as present when the blood pressure was above 140/90 mm. Hg in the last half of pregnancy, usually in the presence of abnormal edema and/or albuminuria. Blood pressures in the pre-eclamptics reverted to non-pregnant levels in the postpartum period.

The age distribution of these toxemic patients was: 4 were 10 to 15 years; 10, 16 to 20; 7, 21-25; 5, 26 to 30; 8, 31 to 35; 4, 36 to 40; and 3, 41 to 45. Thirty-nine patients were coloured and 2 were white.

There were 12 primigravidas; 8 were gravida 2; 2, gravida 3; 2, gravida 4; and 18 patients were in the gravida 5 to 17 group. Nineteen were married and 22 were single, widowed, separated or divorced.

There was a past history of toxemia in 10 of the 29 multiparous women. In 11 of the 41 toxemia patients, a family history of hypertension was elicited.

TABLE I.—MAXIMUM WEIGHT GAIN IN 41 TOXEMIC PATIENTS

Weight gained (lb.)	*Number*
Unknown	2
<10	6
11 - 20	8
21 - 30	12
31 - 40	6
41 - 50	6
51 - 60	0
61 - 70	1
	41

The maximum weight gains during pregnancy are recorded in Table I. This entity presents a "normal curve" distribution.

Serum uric acid levels were available in 12 cases of toxemia. Only one abnormal value was obtained, indicating the uselessness of this test. Both eclamptics had values within the normal range.

The blood types of these patients occurred with the normal frequency.

Three stillbirths were seen in this series. One was associated with premature separation of the placenta and occurred in a woman with hypertension and superimposed pre-eclampsia. The other two were macerated stillbirths in patients with pre-eclampsia.

TABLE II.—PERSONALITY ASSESSMENT OF 41 TOXEMIC PATIENTS

	Pre-eclampsia	*Hypertension + pre-eclampsia*	*Eclampsia*	*% of total*
Abnormal (trait or traits above 70th percentile)	14	4	1	46%
Borderline abnormal (trait or traits between 61st and 70th percentile)	15	3	1	46%
Normal (all traits below 61st percentile)	3	0	0	8%

M.M.P.I. results in the 41 patients are summarized in Table II. Nineteen personalities had frankly abnormal traits, 19 had borderline abnormal traits, and only 3 personalities were definitely normal. The incidence of each abnormal and borderline abnormal trait is shown in Table III.

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TABLE III.—INCIDENCE OF ABNORMAL AND BORDERLINE ABNORMAL PERSONALITY TRAITS (M.M.P.I.) IN A GROUP OF 41 TOXEMIC PATIENTS

Trait	*Number of occurrences in abnormal range*	*Number of occurrences in borderline abnormal range*
Hypochondriasis	4	7
Depression	2	12
Hysteria	4	6
Psychopathic deviate	7	11
Interests	6	12
Paranoia	0	14
Psychasthenia	1	7
Schizophrenia	6	7
Mania	6	9
Sociability	0	11

No particular abnormal personality pattern appears to predominate.

DISCUSSION

Williams postulated that any theory for the etiology of toxemia to be regarded as acceptable must explain certain clinical and pathological facts,[2] a few of which are: (1) The predisposing influence of the primigravid condition, multiple pregnancies, moles and hydramnios. (2) The increased incidence of the disease in certain geographic areas and among the indigent. (3) The increasing incidence as term approaches. (4) The rarity of repeat eclampsia. (5) The improvement which usually ensues after death of the fetus. (6) The hypertension, edema, albuminuria, convulsions and coma. (7) The characteristic renal and hepatic lesions. No "organic" theory successfully explains the above-listed items, nor has any "toxin" ever been isolated which will predictably produce the disorder.

Previous work with a series of unmarried mothers suggested that the stress of pregnancy which is the sum total of the fear of the unknown and the environmental stresses may, in a susceptible, fragile personality, produce decompensation. The vasospasm, salt and water retention, pathognomonic of pre-eclampsia, may be the result of these disturbed emotions. If an overwhelming, severe decompensation occurs, the generalized "somatic shudder" known as eclampsia may supervene.

Is the psychosomatic theory compatible with the seven clinical and pathological facts mentioned by Williams? Firstly, fear of the unknown as well as a lack of confidence in her ability to deliver successfully is more likely in a primigravida. Moreover, very young and very old primigravidas should be even less confident and so be more susceptible to toxemia. This is found to be the case. Semmens and McGlamory found that the teen-age primigravida was 15 times more prone to develop eclampsia than a primigravida in the so-called reproductive years and that this trend was most evident in the 13- to 17-year-old group. Similarly, the elderly primigravida who must have some misgivings about her ability to deliver successfully has a 21.7% incidence of pre-eclampsia.[4]

Multiple pregnancy, hydatidiform mole and polyhydramnios produce concern in the attending physician which may be subtly transmitted to the patient.

The increased frequency in indigent patients likely reflects decreased knowledge of the physiology of pregnancy and labour. Many superstitions are encountered in this group of people and they seem particularly susceptible to the stories of "well-meaning friends".

The greater incidence as term approaches is perhaps due to the increased duration of the stress.

The rarity of repeat eclampsia is explainable because the fear of the unknown is absent after the first pregnancy.

The improvement in the toxemia which frequently ensues after death of the fetus may support Soichet's theory. He suggests that toxemia occurs because the patient feels guilty in the eyes of the unborn baby. Intrauterine death, at any rate, relieves the woman of some future responsibility and thus diminishes stress. Toxemia has been noted by a reliable observer in association with pseudocyesis.[1] It also occurs post partum when no fetus is present. In the case reported above, the woman thought that she was still undelivered. The writer has also seen toxemia occur post partum when undiagnosed twins were delivered. The woman was mentally prepared for one, but two evidently were "too much".

The characteristic reversible renal lesions described in this disorder[3, 9] may be secondary to vasospasm. Toxemic lesions elsewhere are not specific or invariable[7] and are likely secondary to anoxia and electrolyte imbalance.

SUMMARY AND CONCLUSIONS

Only 3 of 41 toxemic patients, or 8%, were found to have normal personalities as measured by the M.M.P.I. test.

This supports the contention that toxemia of pregnancy is a psychosomatic disorder which results when stress produces personality decompensation in a susceptible person.

The criteria of Williams appear compatible with this theory.

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SPECIAL ARTICLE

THE STRUCTURE OF THE TRABECULAR MESHWORK IN RELATION TO THE PATHOGENESIS OF OPEN ANGLE GLAUCOMA*

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"RESEARCH is to see what everybody has seen and to think what nobody else has thought." These words of Szent-Györgyi are particularly pertinent to the investigation to be described in this report. It is a morphological study of a very small but important part of the eye which has already been the subject of many detailed examinations.

Open angle glaucoma is characterized clinically by an elevation of intraocular pressure in association with loss of visual field, due to atrophy and cupping of the optic nerve head. Elevation of intraocular pressure precedes loss of vision and if uncorrected results in blindness. Consequently the objective of fundamental glaucoma research is to establish the sequence of events leading to ocular hypertension.

Several approaches have been made to this problem and to understand them it is necessary to refer to the circulation of intraocular fluid (Fig. 1). The fluid content of the eye consists of vitreous, which is static, and aqueous, which is constantly changing. Aqueous is secreted by the ciliary body into the posterior chamber and after entering the anterior chamber through the pupil it must traverse the trabecular meshwork to reach Schlemm's canal. Approximately 30 collector channels conduct aqueous to the scleral plexus which is in communication with the blood vascular system outside the eye. There is a pressure drop in the normal eye of 5 to 10 mm. Hg across this barrier and obstruction to aqueous outflow in glaucoma must occur somewhere in the drainage pathway between the anterior chamber and episcleral plexus.

Physiologists disagree on the proportion of the total resistance to outflow which exists in the meshwork, the canal, and the scleral plexus in normal and glaucomatous eyes. Morphological studies which have attempted to solve this problem are also inconclusive and there persists in the literature a fundamental disagreement regarding the nature of the filtration channels in the trabecular wall of Schlemm's canal. There are those who believe that aqueous enters the canal through large pores which were first described by Sondermann,[1] whereas other investigators have failed to find openings into the canal[2] and believe that aqueous "squeezes between the endothelial membranes" surrounding the collagen fibres of the meshwork. If there are no direct openings, it is difficult to account for the passage of particulate matter such as latex spheres, and red blood cells from the anterior chamber into the canal.

There have been several recent pathological reports which implicate the trabecular meshwork as a possible site of obstruction in glaucoma.[3-6] Also a new concept of the pathogenesis of congenital glaucoma has been published, based on a developmental abnormality in the meshwork.[7] Barany's demonstration that resistance to outflow can be reduced by adding hyaluronidase to perfusing solutions has stimulated an intensive search for mucopolysaccharides in the outflow pathway.[8] The trabecular meshwork has been considered to be the most likely site of action of this enzyme.

In view of the renewed interest in the trabecular meshwork and the conflicting views on the anatomy of this structure, a further study has been made to establish accurate criteria for the normal morphology of this portion of the drainage pathway in order that pathological changes which might be of significance in the pathogenesis of chronic simple glaucoma may be assessed with greater confidence.

MATERIAL AND METHODS

Human material used consisted of premature baby eyes from six months to term and infant eyes obtained from the eye bank. Adult eyes were used which contained small malignant melanomas. When it became necessary to achieve *in vivo* fixation, rabbit, cat and monkey eyes were used.

In the past the trabecular region has been studied principally by means of paraffin sections cut in a variety of planes (Fig. 2). In this study the meshwork was dissected in layers from the anterior chamber to Schlemm's canal and teased fragments of whole fibres were examined as wet preparations. This technique avoids many artefacts introduced by imbedding and sectioning, preserves third-dimensional relationships, and permits a detailed study of individual whole fibres.

This paper will present, initially, some observations on the normal structure of the drainage pathways with particular reference to the trabecular wall of Schlemm's canal, following which it will illustrate certain proliferative and degenerative changes in individual trabecular fibres which may be of significance in the etiology of glaucoma.

1. *The Structure of the Drainage Channels in the Infant and Adult Meshwork*

The trabecular meshwork has been divided into an inner *uveal* portion and an outer *corneoscleral* portion. The uveal meshwork consisted of a lace-

*The research reviewed in this paper was awarded the Bronze Medal of the Royal College of Surgeons of Canada for 1960 and was presented at the annual meeting of the College in January 1961.

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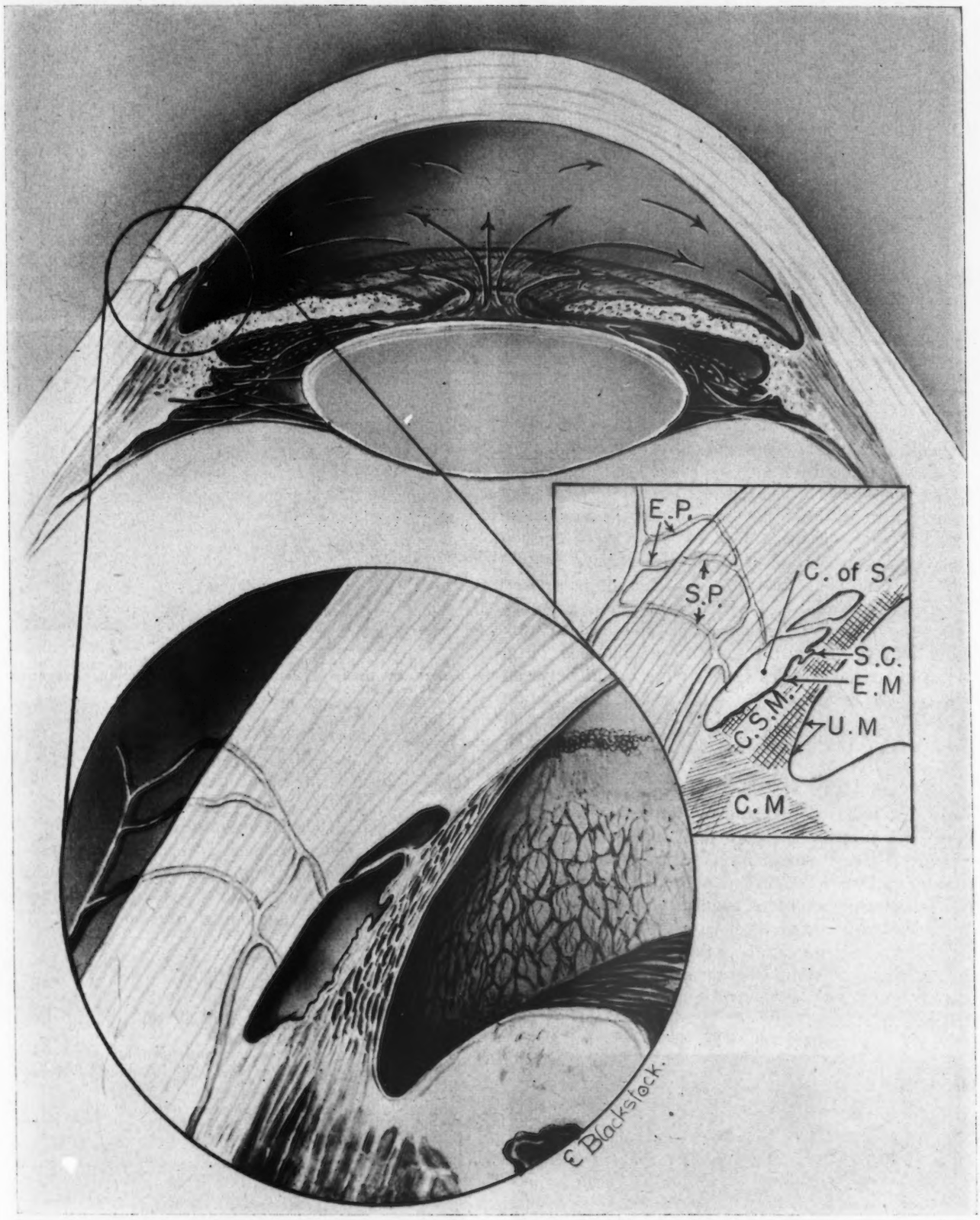

Fig. 1.—Drawings, showing the pathways utilized by aqueous in escaping from the anterior segment of the eye. (C.M.) ciliary muscle, (C. of S.) canal of Schlemm, (C.S.M.) corneoscleral meshwork, (E.M.) endothelial meshwork, (E.P.) episcleral plexus, (S.P.) scleral plexus, (S.C.) Sondermann's canal, (U.M.) uveal meshwork.

like network of collagen fibres which were attached on one side of the filtration angle to the root of the iris and which, on the other side, terminated in Descemet's membrane (Fig. 3). There were large openings between the fibres through which aqueous could travel readily to the deeper layers. In the fetal and infant eye the openings were much smaller, showing that considerable growth must take place before the porosity of the adult meshwork is attained.

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Fig. 5.—Flat preparation showing clumps of pigment in the corneoscleral drainage channels in an infant. (Human, polychrome methylene blue stain, × 1500.)

The corneoscleral meshwork consisted of sheets of collagen which were lined by endothelial cells and perforated by many oval and spiral openings. Near Schlemm's canal the collagen lamellae were much thinner and the meshwork became more cellular. The gaps between lamellae were crossed by fine intercellular bridges, and many of the spaces resembled vacuoles. Red blood cells were frequently found in the clefts, and pigment granules were deposited on the cytoplasm showing that bulk flow had occurred through these channels (Fig. 4). Similar but smaller spaces were found between the corneoscleral lamellae in the infant, which again draws attention to the growth and differentiation which takes place in the meshwork with increasing age (Fig. 5).

The trabecular wall of Schlemm's canal is an area which has defied analysis for many years. In ordinary paraffin sections the wall of the canal appeared intact except for occasional large defects known as Sondermann's canals (Figs. 1 and 2). Nevertheless, when blood regurgitated into the canal it passed with the greatest ease into the meshwork in places where no canals of Sondermann existed. It is apparent that some easy means of intercommunication must exist between the canal and the intertrabecular spaces.

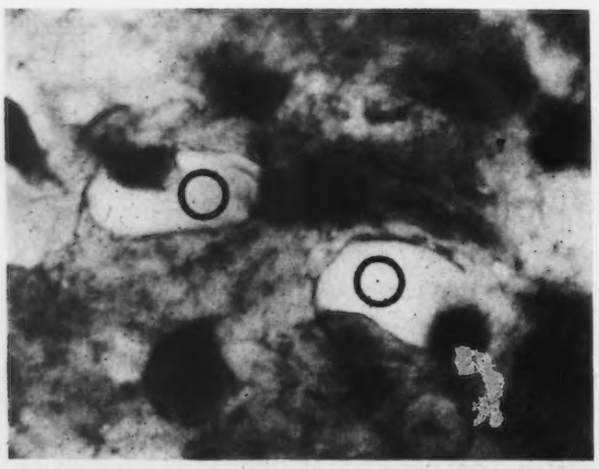
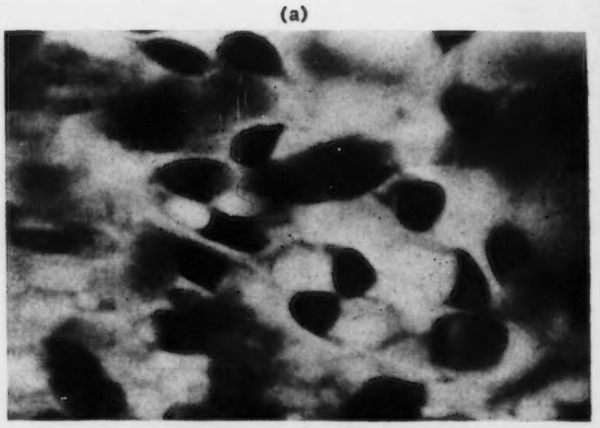


Fig. 7.—Flat preparation showing large openings (o) in the trabecular wall of Schlemm's canal. (Human, Rinehart stain, × 1250.)

(a)



(b)

Figs. 8 (a, b).—Flat preparations showing spaces in the endothelial lining of Schlemm's canal. (Human, polychrome methylene blue stain, (a) × 750, (b) × 1500.)

Flat preparations of the trabecular wall of the canal were made to help solve this problem.[9] These showed three features of interest: (1) large grooves (Fig. 6), (2) large openings (Fig. 7), and (3) spaces in the endothelial lining of the canal (Figs. 8a, b). The grooves in the wall of the canal most probably are responsible for the defects in paraffin sections which Sondermann thought were openings into the meshwork. The

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Fig. 2.—Paraffin section showing the anatomical relationships at the filtration angle. (Monkey, Mallory stain, × 40.)

Fig. 3.—Flat preparation showing openings in the adult uveal meshwork. (Human, polychrome methylene blue stain, × 40.)

Fig. 4.—Paraffin section showing red blood cells and pigment granules in the drainage channels of the corneoscleral meshwork. (Human. Mallory stain, × 400.)

Fig. 6.—Flat preparation showing deep grooves in the trabecular wall of Schlemm's canal. (Human, Rinehart stain, × 200.)

Fig. 10.—Flat preparation showing eosinophilic casts of several channels in the endothelium lining the trabecular wall of Schlemm's canal. (Human, polychrome methylene blue stain, × 400.)

Fig. 12.—Flat preparation showing distribution of acid mucopolysaccharide in normal uveal fibres. (Cat, Rinehart stain, × 400.)

Fig. 17.—Flat preparation of a corneoscleral fibre showing diffuse thickening of the clear zone. (Human, polychrome methylene blue stain, × 400.)

Fig. 19.—Flat preparation of a uveal fibre showing increased staining of the fibre bundles in the clear zone which form thick bands. (Human, polychrome methylene blue stain, × 400.)

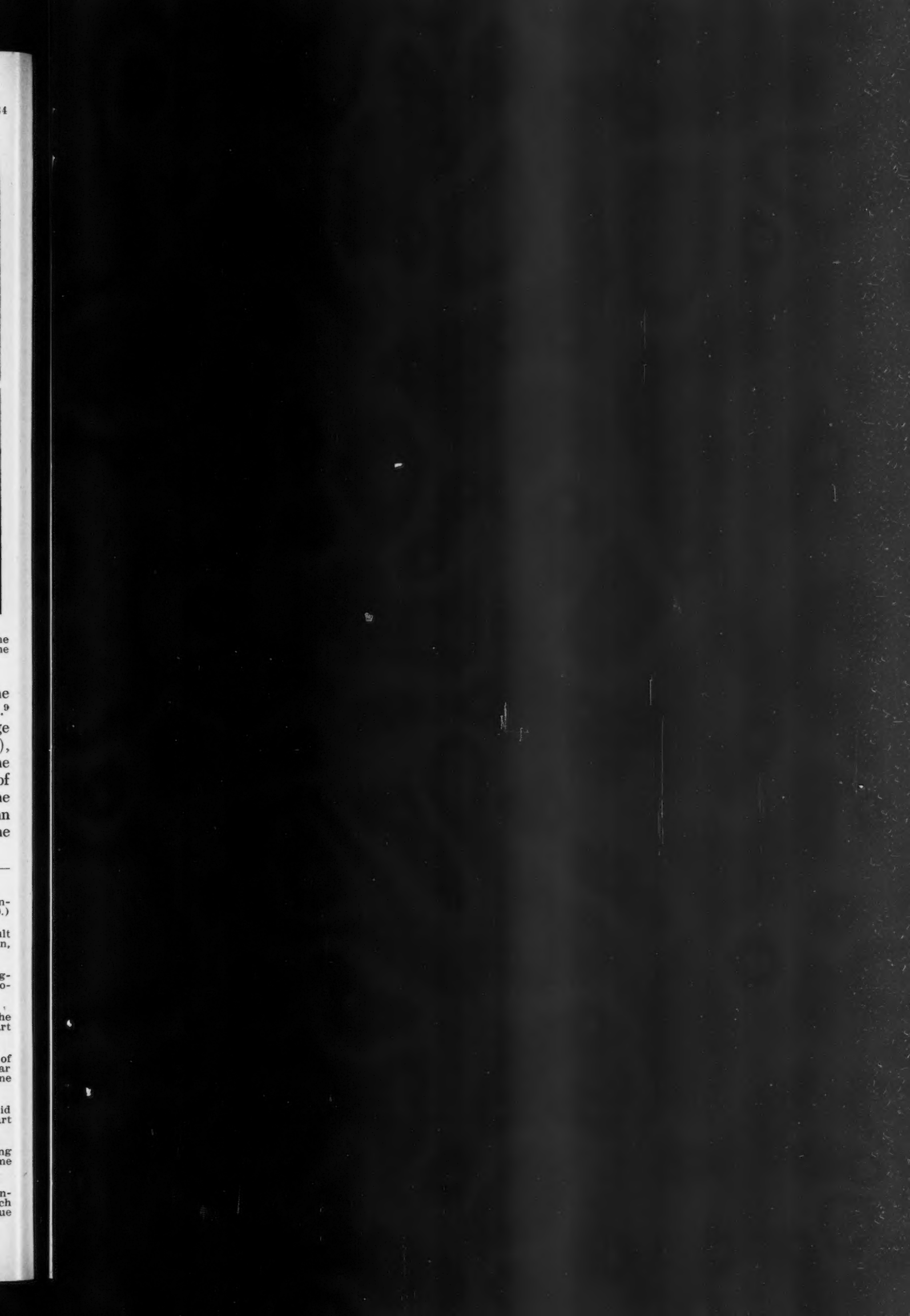


Fig. 2

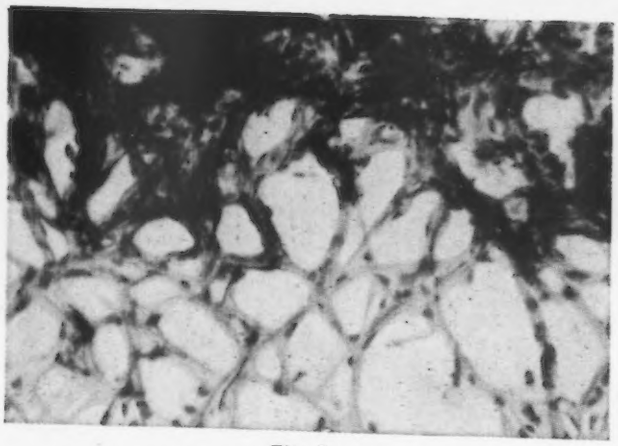


Fig. 3

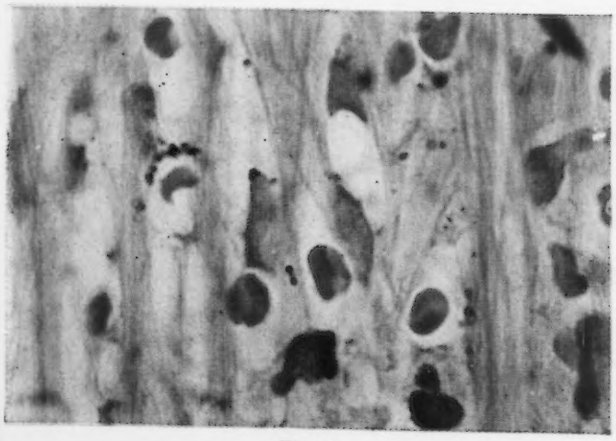


Fig. 4

Fig. 6

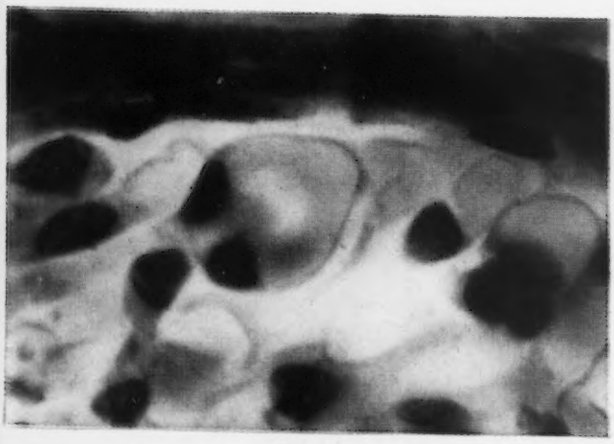


Fig. 10

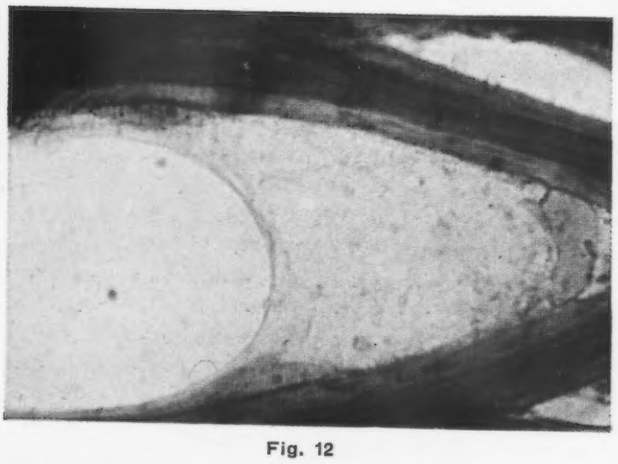


Fig. 12

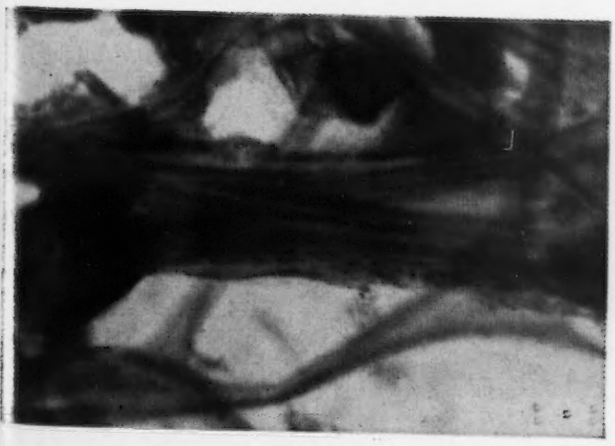
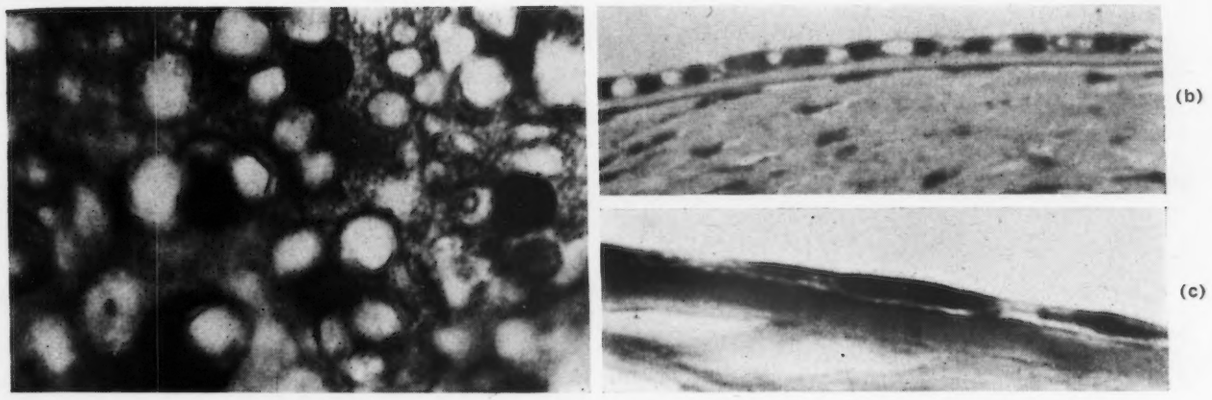


Fig. 17

Fig. 19



Figs. 9 (a-c).—Flat preparation (a) and paraffin sections (b, c) showing the effect of delayed fixation (a. b) and rapid fixation (c) on the formation of vacuoles in the corneal endothelium. ((a) Human, Rinehart stain, × 950; (b) Human, hematoxylin and eosin stain, × 200; (c) Monkey, Mallory stain, × 1500.)

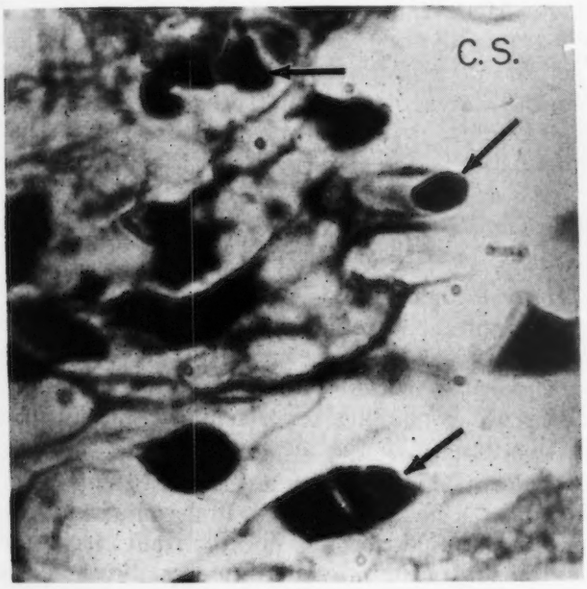


Fig. 11.—Paraffin section showing red blood cells (arrow) trapped at various levels in the channels leading from the meshwork into the canal of Schlemm (C.S.). (Monkey, Mallory stain, × 1500.)

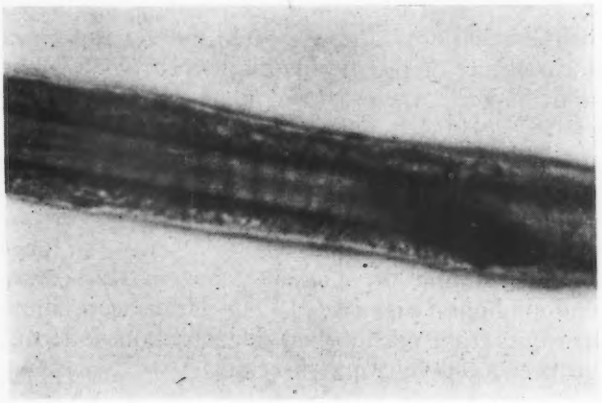
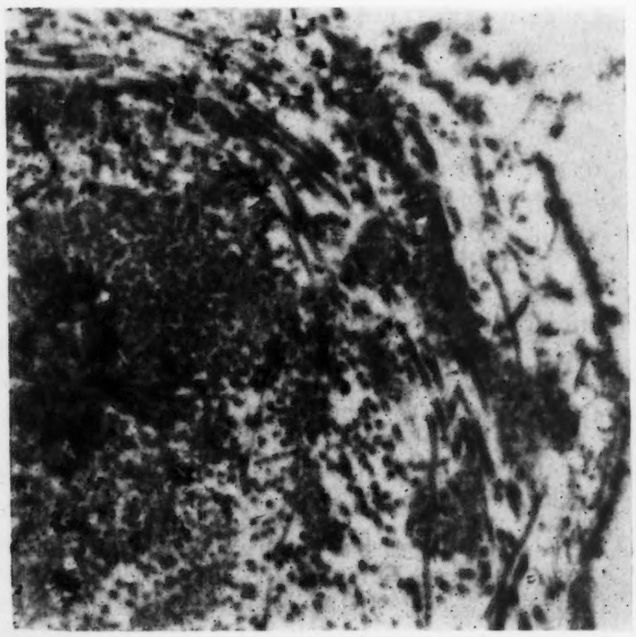
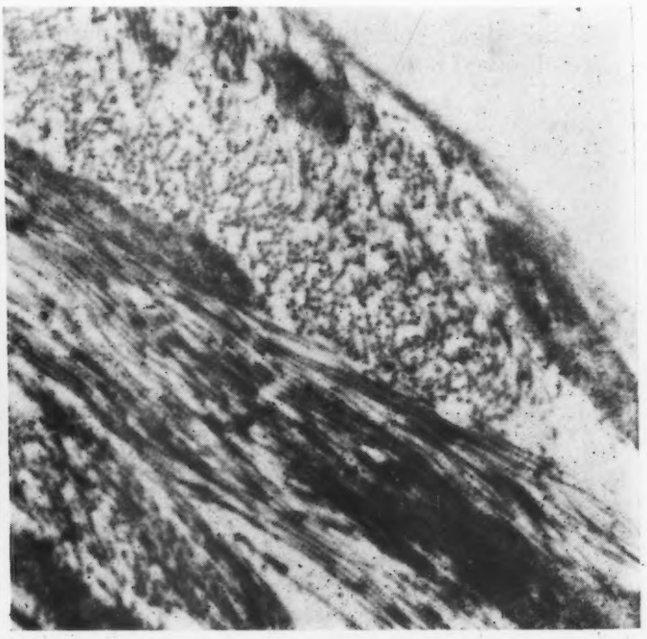


Fig. 13.—Flat preparation of uveal fibre showing an outer layer of endothelium and a subendothelial clear zone in which spiral fibre bundles can be seen surrounding the central collagen core. (Cat, polychrome methylene blue stain, × 950.)

Fig. 14 (below) (a, b).—Electron microphotographs of uveal fibres showing the distribution of primary collagen fibrils in the clear zone and core, (a) in cross section, (b) in oblique section. (Human, (a) × 25,000, (b) × 15,000.)



(a)



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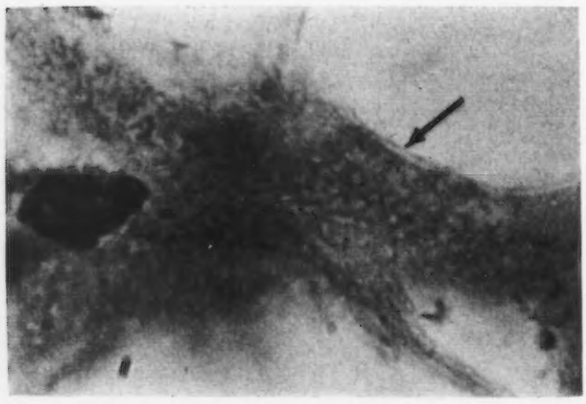

Fig. 15.—Optical section through the surface of a corneoscleral fibre showing many granules and S-shaped filaments in the clear zone (arrow) which surrounds the collagen core. (Human, polychrome methylene blue stain, × 1500.)

large openings in the flat preparations of the wall of the canal are another manifestation of the plexiform nature of the meshwork in this region. Rohen and Unger[10] have shown that occasional large canals lie buried within the meshwork and these may enter the canal of Schlemm through these large openings. The spaces in the endothelial lining of the canal were originally thought to be postmortem vacuoles,[11] and this view was reinforced by the finding of similar spaces in the corneal endothelium (Figs. 9a-c). The latter were shown to result from postmortem degeneration and could be prevented by rapid fixation.

Identical spaces were discovered in the trabecular wall of the canal in the monkey and these persisted when rapid fixation *in vivo* was employed, which prevented the degenerative changes in the corneal endothelium.[12] This observation has been repeated, using human eyes which were fixed immediately after enucleation. It became apparent that the spaces in the endothelial lining of the canal could be channels *between* cells rather than spaces *within* cells and this possibility was investigated further.

Under direct observation, India ink particles were observed flowing through a space from within the meshwork. Casts of the channels have been found which presumably formed when blood plasma regurgitated into the canal of Schlemm before clotting (Fig. 10). Flat preparations and tangential paraffin sections showed red blood cells trapped at various levels in the channels as they penetrated the endothelial lining of the canal into the meshwork (Fig. 11).

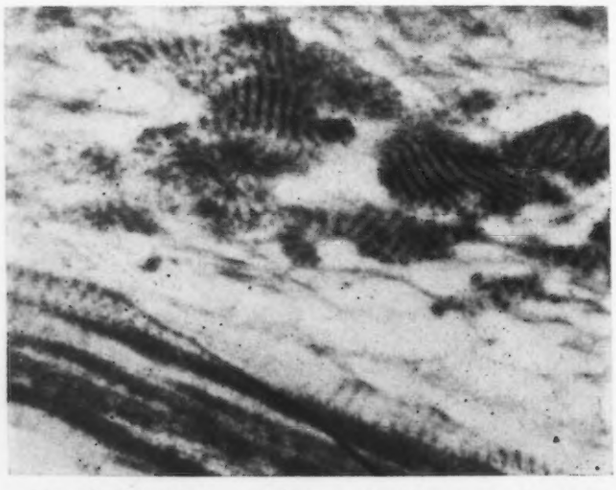

Fig. 16.—Electron microphotograph of a corneoscleral fibre showing macrocollagen bundles in the clear zone which surrounds the collagen core. (×.20,800.)

These observations provide good evidence that the spaces in the endothelium lining the wall of the canal are channels which, in the living eye, are the final portion of the outflow pathway utilized by aqueous in reaching the canal of Schlemm. From flat preparations the size, frequency and spiral course taken by these channels can be determined. Serial optical sections have been used to construct models of individual channels and these have been combined in a composite model to illustrate their spiral course and interrelationships, in three dimensions. In order to draw attention to this portion of the outflow pathway and emphasize its principal structural component, it has been named the *endothelial* meshwork.[12]

2. *The Distribution of Mucopolysaccharides in the Trabecular Meshwork*

If hyaluronic acid is present in the meshwork, it is important to establish whether it is deposited on the surface of fibres in the drainage pathways or is located within individual trabecular fibres. There are conflicting reports in the literature on its distribution in the meshwork.[13-15]

Acid mucopolysaccharides stain a blue colour with the Rinehart colloidal iron stain and it is unfortunate that no more specific stain is available to demonstrate individual mucopolysaccharides such as hyaluronic acid. An examination of individual fibres showed a yellow-green outer layer of cytoplasm, a blue, subendothelial mucopolysaccharide-rich clear zone, and a dense orange collagen core (Fig. 12). No evidence of blue-staining material has been found on the surface of the fibres, unless the endothelium was disturbed in the preparation of the specimen, thus exposing the mucopolysaccharide inside the fibre. For this reason broken fibres stained an intense blue.

The reports of hyaluronidase-sensitive material within the drainage pathways appear to be based on the observation of fragmented fibres or pooling of stain. It was not possible to demonstrate a hyaluronidase effect on the staining properties of whole fibres. Consequently this investigation does not clarify Barany's observations on the effects of hyaluronidase on outflow resistance.

3. *Proliferative and Degenerative Changes in the Trabecular Meshwork*

For many years Salzmann's[16] description of the microscopic structure of individual trabecular fibres has been accepted, but recently, as a result of electron microscopic studies, his classical concepts

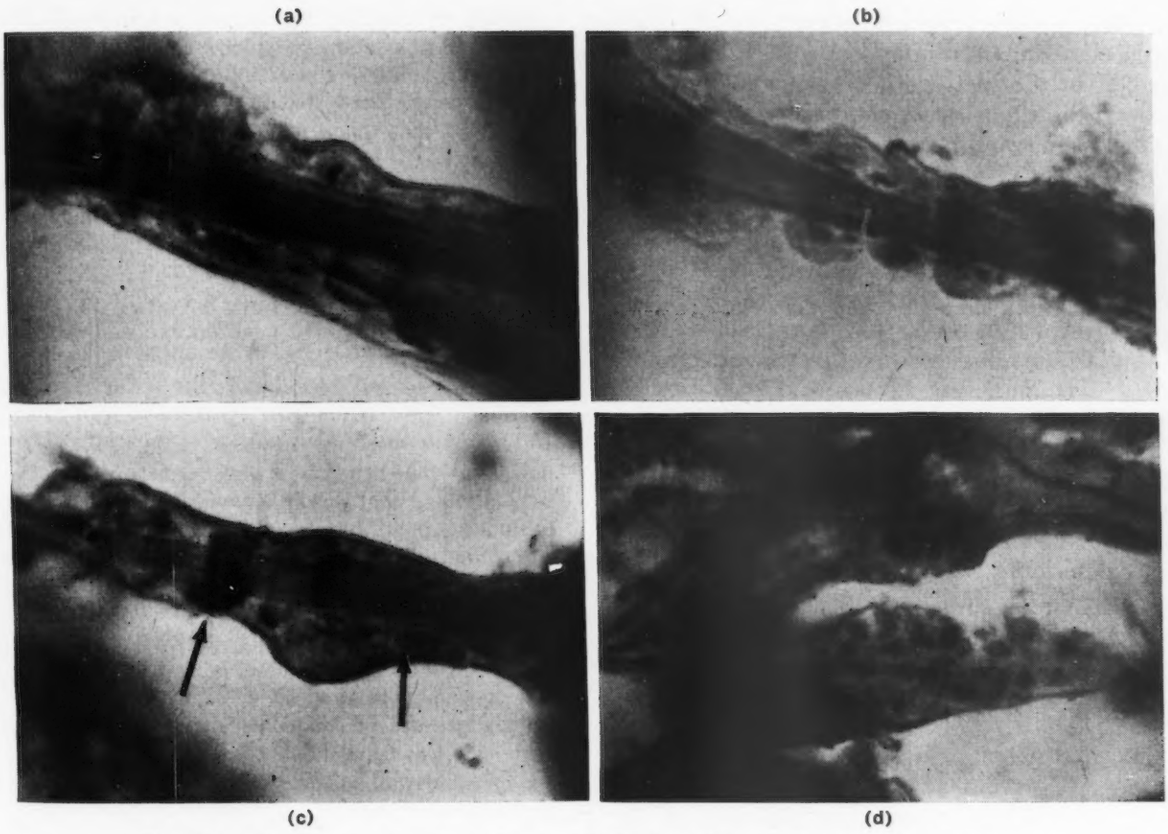

Fig. 18 (a-d).—Flat preparations showing thickening of uveal fibres (a, b, c) and corneoscleral fibres (d) as a result of collagen fibre bundle proliferation in the clear zone. Some of the fibre bundles have fused (arrow) to form thick bands. (Human, polychrome methylene blue stain, × 1500.)

have had to be modified. Salzmann divided the components of each fibre into four layers: (1) an outer endothelial layer, (2) a subendothelial clear zone which Salzmann believed to be a structureless glass membrane, and (3) an inner collagen core surrounded by (4) a layer of elastic fibres. The principal modification of Salzmann's original concept concerns the clear zone in which Garron and his colleagues[17] have found primary collagen microfibres which possessed an unusual 1000 A.U. banding.

Teased preparations of uveal fibres demonstrated the basic structural components described by Salzmann and in addition, with the light microscope, many fibre bundles could be seen in the clear zone which had a spiral configuration around the central collagen core (Figs. 12 and 13). The latter were more conspicuous in electron microphotographs (Figs. 14a, b).

In normal corneoscleral fibres it was difficult to identify the clear zone. However, optical sections through the surface of the fibres showed numerous granules surrounding the collagen core. In suitable preparations the granules could be resolved into tightly coiled spirals (Fig. 15), which corresponded in position to the macrocollagen bundles found in the clear zone in electron microphotographs (Fig. 16).

Proliferative and degenerative changes took place in the fibre bundles which surround the central collagen core in both uveal and corneoscleral fibres. The proliferative changes which occurred may produce a diffuse thickening or a localized annular or nodular expansion of the clear zone (Figs. 17 and 18a-d). The degenerative changes consisted of a fusion of several fibre bundles to form a more darkly staining hyaline-like band or spiral filament (Fig. 19).

Similar nodular and annular expansions of the clear zone were seen in a glaucomatous eye which was studied three years ago at the Institute of Ophthalmology in London, England.[18] Garron[19] has also reported thickening of the clear zone in a case of glaucoma but could not be certain of the specificity of this finding for glaucoma.

4. *Relationship of Observations to the Pathogenesis of Open Angle Glaucoma*

It is clear that earlier pathological examinations of the trabecular meshwork in glaucomatous eyes have been inadequate because knowledge of the normal anatomy has been incomplete. For example, the term "foamy degeneration" has been applied to regions in the meshwork which show a cystic vacuolated appearance. Some of the changes described may be the result of poor sectioning, whereas others correspond to areas where attenuated cytoplasmic strands and fibres fill the clefts between lamellae. This is a normal finding easily demonstrated in human and monkey eyes in flat preparations.

Swelling, proliferation and atrophy of the endothelial cells, and trabecular sclerosis have all been described in the meshwork of glaucomatous eyes. However, the difficulty in comparing exactly equivalent areas in two different eyes in paraffin sections and the great variation in the morphology of normal structures in the same eye throw doubt on the importance of these findings.

In this study the primary purpose has been to establish adequate criteria for the normal anatomy of the meshwork in order that morphological findings in glaucomatous eyes may be more accurately assessed. The channels in the endothelial meshwork have only recently been described and it is possible that pathological changes in this region have been overlooked in the past. The spiral configuration, angulation, size and number of these channels may prove to be important factors which help to determine the resistance to outflow.

In 1956 Ashton and his colleagues[20] concluded from their study of the meshwork that "no correlation was found between the histological appearance and the age of the patient". The investigation described in this report has shown, however, that there may be definite thickening of the trabecular fibres in eyes removed from older persons, as a result of proliferation and degeneration of the fibre bundles in the subendothelial clear zone. The thickening may assume a variety of forms and varies in extent from one eye to another.

These changes have only been seen so far in the uveal fibres and innermost corneoscleral lamellae. They are not specific for glaucoma, nor are they the result of increased intraocular pressure, as they occurred to the most marked extent in an eye which was normotensive prior to removal. Should the dystrophy progress throughout the meshwork, one would expect alterations in the elasticity of the fibres and a reduction in the calibre of the drainage pathways which could lead to increased outflow resistance and an elevation of intraocular pressure. An examination of additional glaucomatous eyes should help to clarify the significance of this concept.

SUMMARY

A comparison between the trabecular meshwork in the fetal and adult human eye shows that as growth proceeds there is enlargement of the spiral and circular openings in the inner cell membranes which divide the anterior chamber from Schlemm's canal. In the outer layers of the meshwork clefts form between the collagen skeleton which are partly filled by "spongy" cytoplasm and crossed by numerous filamentary cytoplasmic strands. Delay in the differentiation of passages between the cells in the trabecular meshwork near Schlemm's canal may be responsible for cases of congenital glaucoma.

Numerous openings up to 6 μ in diameter have been found in the endothelial lining of Schlemm's canal. They are the exit point of spiralling channels 10 to 20 μ in length, which communicate with the meshwork and represent the final pathway taken by aqueous in reaching the lumen of the canal. Many of the channels contain red blood cells, plasma casts and pigment granules, which indicates that bulk flow occurs through these structures in the living eye. It is suggested that this area be designated the *endothelial meshwork*.

Acid mucopolysaccharide could not be demonstrated within the drainage channels of the trabecular meshwork but was found *inside* the trabecular fibres between the fibre bundles of collagen.

Fibre bundles in the inner layers of the trabecular meshwork may undergo proliferative and degenerative changes in normotensive eyes which result in diffuse and localized expansions of the clear zone. These changes appear to increase with the age of the patient and may impair aqueous outflow if they extend throughout the meshwork.

It is hoped that this study will lead to more intensive evaluation of the trabecular meshwork as a possible site of resistance to aqueous outflow. If it can be definitely established that in primary glaucoma the initial pathological changes occur in this portion of the outflow pathway, more successful therapy may result.

I am grateful for the many facilities and opportunities made available at the Institute of Ophthalmology in London, England, and at the University of Toronto. I am particularly indebted to Professor Norman Ashton and Professor A. J. Elliot for their advice and encouragement and to Dr. T. Leeson for preparing the electron microphotographs.

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CASE REPORTS

EPIDERMOID CYST OF THE CECUM

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THE RARE occurrence of an epidermoid cyst of the cecum is reported in the following case history.

Mrs. R.W., a 22-year-old woman, was admitted to hospital on August 23, 1960, for investigation of a right lower abdominal mass which had been discovered accidentally. Her last normal menstrual period occurred on August 5, 1960, and she had noted no abnormality regarding her menstrual cycle. She was asymptomatic and afebrile.

In 1945 she had had a tonsillectomy and adenoidectomy. In 1948 appendectomy was performed for acute appendicitis. In 1955 she was ill in hospital for a period of two weeks with infectious mononucleosis.

On examination she appeared to be healthy. The only significant finding was a smooth, round, mobile, non-tender mass, the size of an apple, which was palpable in the right lower quadrant of the abdomen.

Urine was normal. Her hemoglobin value was 12.2 g. %, and her leukocyte count was 8300 per c.mm. with a normal differential count. Her erythrocyte sedimentation rate was 38 mm. per hour and her stools were repeatedly negative for occult blood. The chest roentgenogram and cholecystogram were normal. Intravenous pyelograms revealed functioning kidneys. There was a visible soft tissue mass, moderately well outlined, 9 cm. in diameter, located above the right iliac crest. The barium enema showed a defect on the medial wall of the cecum at the site of the soft tissue mass.

On August 29, 1960, a laparotomy was performed through a right para-umbilical incision. The mass was located in the mesentery at the ileocecal angle and was the size of a fist. It was somewhat lobulated and doughy in texture with a smooth serosal surface. There were several soft, rather friable lymph nodes along the course of the right colic vessels. Because the mass was inseparable from the wall of the cecum, and also because at the time the possibility of malignant disease could not be excluded, a right hemicolectomy was performed. Lymph nodes along the right colic vessels were enlarged up to 4 cm. in diameter. There was an uneventful recovery.

The operative specimen consisted of the cecum, 15 cm. of the ascending colon and a section of the terminal ileum 9.5 cm. in length. A large mass, measuring 10 cm. x 7 cm. x 4 cm., was situated in the anterior wall of the cecum. The mass was completely intramural. The mucosal surface of the ileum and colon was soft and velvety, with no gross abnormality. The mass encroached on the lumen of the bowel but did not obstruct it. It was enclosed in a capsule of whitish membranous tissue measuring up to 0.2 cm. in thickness; the mass itself was a cystic structure composed of whitish friable, pulpy material. The inner surface of its capsular membrane was smooth and shiny. It was not possible to identify the appendiceal stump. Microscopic examination revealed that the cyst was lined by squamous epithelium. Fifteen lymph nodes attached to the pericolic fat showed reactive hyperplasia only. The pathological diagnosis was: "Epidermoid cyst lined by squamous epithelium".

DISCUSSION

Mesenteric cysts have been regarded as the rarest of abdominal tumours by various authorities.[1, 2] Warfield[2] in 1932 reviewed the literature and found 129 reported cases since 1920. Steinreich,[3] in 1955, reported eight cases in a ten-year period amongst 444,332 hospital admissions. Hinshaw[4] in 1957 reported a case of unattached cysts in the peritoneal cavity of a 23-year-old woman. These were thin-walled structures, 4 cm. to 5 cm. in diameter, containing clear white fluid. No other cases of this type have been reported to date, nor does the literature contain any reference to the occurrence of epidermoid cysts involving the cecal wall as in the case described in this report. The latter, too, may be considered to be one of the rarest of abdominal tumours.

Dermoids of the mesentery apparently arise from the ovary, as suggested by Warfield.[2] Apart from the proximity of the cecum to the right ovary, there was no evidence that the latter was the site of the lesion in our patient. According to Warfield, dermoids of the mesentery always occur in females. Remnants of ovarian tissue may well have been displaced to the region of the cecum during its embryonic development in this case.

Mesenteric cysts may give rise to such complications as necrosis, torsion, hemorrhage, rupture, volvulus, intussusception, bowel occlusion, peritonitis and malignant change. It is possible that some of these complications may in time have affected the patient described in this report.

SUMMARY

A case of epidermoid cyst of the cecum is reported. Heretofore, this rare abdominal tumour has not been described in the literature.

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A WEAK B RED CELL ANTIGEN CO-EXISTING WITH SERUM ANTI B ANTIBODY*
REVIEW OF LITERATURE AND INVESTIGATION OF A CASE

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VARIANTS of the B red cell antigen are rare but of considerable importance, since they may lead to erroneous blood groupings and the dangers of a mismatched transfusion.

There are no established subgroups of the B antigen comparable to the A_1, A_2 etc. divisions of the A antigen, although in 1955, Moullec, Sutton and Burgada[1] reported a weakly reacting B antigen which they called B_3. The phenotype Bw was described in 1958 by Levine *et al.*[2] as a weak B antigen, genetically determined, which gave only microscopic agglutinates with potent anti B sera. A similar, but weaker, B antigen called Bx was described by Dunsford, Stacey and Yokoyama[3] in 1957. In none of these instances was there an anti B in the serum.

In 1959, simultaneous reports by Cameron *et al.*[4] and Giles *et al.*[5] described a few instances in which a weak B antigen and an isoagglutinin anti B were present in the same individual. A normal A antigen was also demonstrable and the phenotype $A_1{}^b$ was suggested for this unusual blood group. Investigation revealed that this b antigen was demonstrable with some but not all anti B sera and that it appeared to be an acquired characteristic. These individuals were non-secretors of B substance, and family studies failed to show a similar red cell antigen. It is interesting that six of the 10 patients described in these reports had cancer.

Andersen,[6] in 1959, reported a family study on individuals of Groups $A_1{}^b$ and $A_2{}^b$, presenting convincing evidence that, in some instances at least, this was an inherited characteristic. In one of the families studied, two siblings were found to have the b antigen.

A 63-year-old woman was admitted to the Vancouver General Hospital in September 1960 with pelvic metastases from carcinoma of the body of the uterus and large bowel obstruction. Transverse colostomy was carried out.

She gave a past history of pelvic inflammatory disease following delivery of twin sons in 1937. In 1953 bilateral stripping of varicose veins and left fasciotomy were performed for stasis ulceration of the legs. In May 1960 carcinoma of the body of the uterus was diagnosed by cytological examination. This was treated by radium insertion and panhysterectomy in June 1960.

TABLE I.

	Anti B	*Anti A*	*A cells*	*B cells*	*Saline anti D*	*Albumin anti D*
Tile	+ (wk)	++++	—	+++		
Tube	+ (wk)	++++	—	+++	+	+

The patient denied having received a blood injection or transfusion at any time during her life, and thorough questioning failed to elicit any history of a twin.

On September 7, 1960, at the time colostomy was performed, a request for 1000 c.c. of blood was received at the Vancouver General Hospital Blood Bank. The results obtained on this patient's routine grouping are shown in Table I.

The patient's cells reacted strongly to anti A and weakly to anti B grouping serum. The patient's serum reacted normally with pooled group B cells, indicating the presence of a normal anti B in her serum, but there was no reaction with pooled A cells.

Cross-matching with A positive blood proved satisfactory but the patient's operative and postoperative course did not warrant the administration of blood.

It was felt that there were four possible explanations for the grouping results shown in Table I. The possibility of a blood group chimera was considered; however, the patient gave no history of a twin. Recent blood transfusion with persistence of red cell antigen and/or antibodies might also account for such a result, but it is known that the patient did not receive a blood transfusion prior to her last admission to hospital. That this could be an inherited characteristic seemed a definite possibility in view of Andersen's[6] work, while the reports of Cameron *et al.*[4] and Giles *et al.*[5] favoured an acquired characteristic.

INVESTIGATION

Random anti B sera from group A individuals were incubated with pooled group A cells, group B cells and the patient's cells at room temperature for one hour and were read macroscopically after centrifugation. The results, shown in Table II, indicate the ability of the patient's b antigen to react weakly or not at all with various anti B sera.

Table III shows the same anti B sera titred out against the patient's cells and normal pooled B cells. The low titre reactions of the patient's cells as compared with the controls tend to reaffirm the weak nature of the b antigen and also show that the reactivity is independent of the saline titre of the anti B antisera.

The family study included twin sons, two sisters and one brother. The results, shown in Table IV, failed to reveal any evidence of a b antigen.

TABLE II.

Anti B serum	*Pooled A cells*	*Pooled B cells*	*Patient's cells*
No. 1	—	++++	++
2	—	++++	—
3	—	+++	—
4	—	++++	—
5	—	+++	—
6	—	++++	+
7	—	++++	+
8	—	++++	—
9	—	++++	++
10	—	++++	—

*From the Blood Bank Division, Department of Pathology, Vancouver General Hospital, Vancouver, B.C., and the Department of Medicine, University of British Columbia, Vancouver, B.C.

TABLE III.—4% SUSPENSION OF PATIENT'S RED BLOOD CELLS

Anti B serum	*Titre* 1	2	4	8	16	32	64	128
1	+	+	—	—	—	—	—	—
2	++	++	+	—	—	—	—	—
3	+++	++	++	+	—	—	—	—
4	—	—	—	—	—	—	—	—
5	++	+	—	—	—	—	—	—
6	+	+	—	—	—	—	—	—
7	++	+	—	—	—	—	—	—
8	++	+	—	—	—	—	—	—
9	—	—	—	—	—	—	—	—
10	—	—	—	—	—	—	—	—

Anti B serum	*4% Suspension of pooled B cells* 1	2	4	8	16	32	64	128
1	++++	++++	+++	+++	++	+	+	(+)
2	++++	++++	+++	+++	++	(+)	—	—
3	++++	++++	++++	++++	+++	++	+	+
4	++++	++++	+++	+++	++	+	+	—
5	++++	++++	++++	+++	+++	++	+	+
6	++++	++++	+++	++	+	+	(+)	—
7	++++	++++	+++	++	+	+	(+)	—
8	++++	++++	+++	+++	++	+	(+)	—
9	++++	++++	+++	++	++	+	—	—
10	+++	++	++	+	—	—	—	—

Saliva inhibition tests (Mollison[7]) carried out on the patient and her relatives showed all to be secretors of A substance. Tests for B substance in the patient's saliva were negative (Table V).

TABLE IV.

	Anti B	*Anti A*	*A cells*	*B cells*	*Anti D*	*Anti A_1*
Sister	—	+	—	+	+	+
Sister	—	+	—	+	+	+
Son	—	+	—	+	+	+
Son	—	+	—	+	+	+
Brother	—	—	+	+	+	—

Genotyping of the patient and her relatives was carried out by the Ortho Research Foundation. The results shown in Table V confirmed the patient's weak b antigen and failed to show a similar antigen amongst members of her family.

DISCUSSION

There seems little doubt that the b antigen in this patient's red cells differs from the normal B antigen in strength of reaction with anti B sera and in failure to react with some high-titre anti B sera. It can be further assumed that a b antigen which can coexist with serum anti B must, indeed, differ from the normal B antigen. This patient, although a secretor of A substance, was not a secretor of B substance and her family lacked a B or b red cell antigen.

The high incidence of cancer among the reported cases of this blood type is interesting although completely unexplained. It is unfortunate that this patient did not have a blood grouping performed earlier in life or before the onset of her cancer so that a comparison of red cell antigens could be made.

CONCLUSION

A 63-year-old woman with cancer was shown to have a normal A antigen, anti B isoagglutinin and also a weakly reacting b antigen, thus fitting into the blood group A^b. There was no evidence to indicate that this was a hereditary characteristic.

TABLE V.—RED CELL ANTIGENS

	Saliva inhibition test	*A*	*B*	*D*	*C*	*E*	*c*	*e*	*K*	*k*	*Fy^a*	*S*	*s*	*P*	*Le^a*	*Jk^a*	*Jk^b*
Patient	Secretor "A" substance, non-secretor "B" substance	+	(+)	+	0	+	+		0	+	+	+	+	+	0	+	+
Sister	Secretor "A" substance	+	0	+	0	+	+	0	0	+	0	+	+	+	0	+	
Sister	" "	+	0	+	0	+	+	0	0	+	0	+	+	+	0	+	
Son	" "	+	0	+	+	+	+		0	+	+	+	+	+	0	0	
Son	" "	+	0	+	+	+	+		0	+	+	+	+	+	0	0	
Brother	Not done	0	0	+	0	+	+	+	0	+	0	+	+	+	+	0	+

The authors wish to thank the Ortho Research Foundation and the Canadian Red Cross Blood Transfusion Service for carrying out genotyping, and Dr. S. Sargent for referring this patient.

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THE PRESENT STATUS OF ENDOCRINE ABLATIVE SURGERY IN METASTATIC BREAST CANCER

IT IS well recognized that breast cancer presents an attractive clinical situation in which to evaluate therapeutic possibilities in view of the chronicity of the disease even after symptomatic metastases have become apparent. In this disease the balance between host resistance and biological activity of the tumour is commonly favourable to prolonged survival. The importance of the environmental situation in which the tumour finds itself is obviously a fundamental consideration, as is the biological development of the tumour itself. The environmental situation may be affected by factors of genetic constitution and immune reaction in the host as well as by the peculiar dependency of breast cancer on circulating sex hormones of steroid type. The maturation of the tumour itself can perhaps be demonstrated by progressive changes in the original heterogeneous tumour cell population towards one of greater homogeneity by which process cells having structural differences in chromosome counts or physiological differences in their metabolic requirements and activities, illustrate persistence of stem line cells and biological degradation of less aggressive cell types.

The dependence of mammary carcinoma on an estrogenic environment is of practical importance and has encouraged a continuing study along such therapeutic pathways as (1) the use of synthetic androgens and estrogens; (2) estrogen deprivation by extirpative surgical procedures; (3) the complementary ablation of other pituitary factors; and (4) the supplementary use of chemotherapy following major extirpative surgery.

In the matter of major endocrine ablations, attention is currently centred on three main problems: (1) the relative indications for adrenalectomy or hypophysectomy; (2) the stage at which such ablative techniques should properly be utilized; and (3) the type of patient for whom these major extirpative procedures should be advised.

Several recent reports warrant appraisal in this regard. A preliminary statement[1] by the Joint Committee of the American College of Physicians and the American College of Surgeons, set up to evaluate adrenalectomy and hypophysectomy, reports the results of these two procedures to be entirely comparable, and an accompanying editorial[2] stresses the fact that there was an impressive biological homogeneity in the two patient populations studied in comparing these two procedures. Not only were the populations similar but the response was almost identical throughout. It was felt that these two ablative procedures produced the same biologic-endocrine alteration and that consequently hypophysectomy could act only by the elimination of adrenocorticotrophic factors. In addition, the percentage of objective remissions was identical (adrenalectomy 31.7%; hypophysectomy 31.3%) and the duration of survival following the surgical procedure was also very similar (adrenalectomy 22.0 months, hypophysectomy 20.6 months).

Consequently the indications for the use of one or other of these procedures would appear not to be related to the results anticipated. The statement that co-operative reports from several contributing institutions produce a pooled cross-section of end results which are representative of results to be expected from any given procedure under nearly ideal conditions, would appear to be warrantned under these circumstances.

A simultaneous report by McCalister *et al.*[3] in the *British Medical Journal* with an accompanying editorial[4] attempts to predict the type of patient in whom a favourable response might be anticipated.

Three factors that were assessable preoperatively seemed to have a major influence on the result. (1) Skeletal metastases either alone or in combination with other metastatic lesions seemed to respond better than local disease or visceral metastases alone. (2) Better results were generally achieved in premenopausal patients and it was quite definitely apparent that the menopause was more important than the age of the patient. (3) It was considered reasonable to assume that the longer the disease was left *untreated* the more likely it was to become independent of hormonal control; certainly the results achieved by ablative surgery were most favourable during the initial six-month period after reactivation of symptomatic metastases.

It should be noted that this last situation concerns a group of "untreated" patients and does not compare results of extirpation with those in a group of patients in whom it might be utilized after they had received other treatment. The best results were apparent in premenopausal patients with osseous metastases, in which group primarily, a 76% objective remission rate was achieved.

Because in this series the age of the patient, the total duration of the disease, and the histology of the tumour appeared to be of no prognostic signifi-

cance, the accompanying editorial[4] quite properly stresses the fact that the total duration of the disease has proved of great significance in other comparable statistics. In this regard, reference is made to the studies of Pearson and Ray[5] in which the free interval between the treatment of the primary disease and the necessity for hypophysectomy is evaluated in relation to the percentage of objective remissions. In this series a free interval of less than a year was associated with a remission rate of 33%, an interval between one and two years with a rate of 47%, an interval between two and four years with a rate of 52%, and an interval over four years with a rate of 66%. In the latter case the remission rate obviously now appears to be weighted in favour of the patient. The editorial also quotes from Pearson and Ray[5] in assessing the value of a previous response to oophorectomy in premenopausal patients. In their series 91% of patients demonstrating an unequivocal objective remission following castration had a second remission after hypophysectomy. Seventy-five per cent with a less obvious remission after castration also demonstrated a second objective remission after hypophysectomy, whereas only 7% who failed to demonstrate a response to castration responded to hypophysectomy.

McCalister *et al.*[3] also attempt an early comparison of the results of immediate hypophysectomy with those achieved by initial simple endocrine therapy followed by hypophysectomy. In their series there is a suggestion that osseous lesions do better with hypophysectomy first, although the authors are careful to stress the fact that the survival period from the start of endocrine therapy of any kind will probably prove to be better with the institution of simple endocrine therapy first, followed by hypophysectomy according to the plan of sequential therapy that has been mentioned previously.

Discussing this same problem of choosing the best time to utilize extirpative procedures, Nelson and Dragstedt,[6] in a paper concerning the use of adrenalectomy and oophorectomy in breast cancer, describe the results in 24 consecutive patients in whom this procedure was used as soon as recurrences appeared beyond the field of mastectomy and radiation therapy. In this series 58% showed an objective remission with an average survival of 44 months, and seven patients were still alive for an average of 60 months after operation. On the basis of this study it was suggested that the operation should be used as soon as the diagnosis of metastatic disease is made. Reference is made in an accompanying editorial[7] to the fact that rapid deterioration is often apparent when growth in dormant metastases is resumed, and it is felt that this is due to the appearance of mutant cancer cells that can grow in the absence of hormones from the ovaries or adrenal glands. According to this editorial, it would seem reasonable to expect such mutants to appear sooner when very large numbers of cancer cells are dividing than when metastases are of microscopic size. If this theory should prove valid, an earlier and more frequent application of endocrine surgery would seem logical.

As noted in the editorial[4] in the *British Medical Journal*, Smithers[8] as well as many others has felt that major extirpations, in which at least 50% of the patients have no worthwhile improvement, demonstrate inadequate dividends when compared with the risk to which the patient is subjected. Therefore, careful selection of candidates for such procedures is mandatory. Unfortunately, the evaluation of estrogen dependency at the time when ablative treatment is being considered remains a problem refractory to solution at the present time.

In attacking this problem Swyer, Lee and Masterson[9] have carried out a careful study of estrogen secretion in patients with breast cancer and have come to the following conclusions: (1) There was no difference in the preoperative estrogen levels in patients who improved and those who did not, following oophorectomy and/or adrenalectomy. (2) Clinical progress was not correlated with any decrease in estrogen brought about by operation. (3) No connection was evident between the histology of the primary tumour, estrogen levels, and the clinical response to adrenalectomy and to oophorectomy.

In this same study 116 vaginal smears were examined and although there was some slight correlation between the overall cytological picture and the urinary estrogen levels, this correlation was of very low order. It became apparent that single occasional smears are not sufficiently accurate to provide a useful indication of estrogenic activity in this group of women.

Possible explanations for this failure to predict accurately the response to estrogen deprivation by studies of this type are offered by the following observations: (1) At the time of gonadectomy, tumours which possibly were once hormone-dependent had by that time become autonomous; and (2) the cellular proliferation in mammary carcinoma depends on attainment of a balance between the production of estrogen and that of the pituitary mammotrophic complex, and when surgery is effective it may succeed simply because it alters this balance.

In the assessment of this important series of papers on management of metastatic mammary carcinoma, it becomes apparent that there is little if any significant difference in the results of adrenalectomy or hypophysectomy. The indications for their use appear identical. The main problems remaining concern the assessment of situations in which there is an indication for extirpative procedures of this type. Fundamentally the decision regarding their use must be made on clinical grounds, on the basis of experience with those patients in whom favourable responses have been achieved by such treatment in the past. A very real difference of opinion exists regarding the stage of the disease in which major extirpation may be

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warranted, and selected series may no longer be considered an adequate means of answering this problem. It would seem that a co-operative study of randomized nature comparing the effectiveness of early hypophysectomy and adrenalectomy against the cumulative longevity achieved by initial simple endocrine measures and subsequent extirpative procedures might constitute a logical extension of further study of this important problem.

N.C.D.

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THE QUEEN ELIZABETH II FUND FOR RESEARCH INTO DISEASES OF CHILDREN

ON JUNE 29, 1959, on motion of the Right Honourable John G. Diefenbaker, Prime Minister of Canada, the House of Commons went into committee to consider the following resolution:

> That in order to mark the occasion of Her Majesty's visit to Canada and her personal interest in the well-being of children, it is expedient to introduce a measure to provide for the establishment of the Queen Elizabeth II Canadian fund to aid in research on the diseases of children, for the purpose of assisting individuals or organizations to undertake or carry on research into the diseases of children and the causes, prevention and treatment of such diseases, and for the payment into the said fund of the sum of $1 million out of the consolidated revenue fund; to make provision for administrative and technical services and facilities required for the purpose of the act; and generally to make such other provisions as may be necessary to accomplish the purpose of the act.

Departing from the usual procedure the House then received and passed, on the same date, three successive readings of Bill C-65 providing for the establishment of the Queen Elizabeth II Fund for Research into Diseases of Children.

In his introduction of the Bill, the Prime Minister emphasized that in order to make this fund widely available for support on the part of Canadians as a whole, and of individuals who choose to contribute to it, provision was made that gifts, bequests, appropriations and other contributions might be donated not only at the time of enactment of this legislation but throughout the years to come.

Under the distinguished chairmanship of Dr. John F. McCreary, Dean of the Faculty of Medicine of the University of British Columbia, the Board of Trustees of the Fund, after lengthy deliberation, concluded that the most efficient means by which these moneys could be utilized would be in the support of physicians dedicated to full-time research in diseases of children. Towards this end, two categories of support were established.

Queen Elizabeth Fellows are selected from applicants who have completed three or four years of graduate training in pediatrics and who intend to continue training in the field of pediatric research. Such Fellows are provided with a stipend of $3500 to $5000 annually in addition to their transportation to any centre in the world which they may select for their training, provided that the quality of pediatric research in that centre meets the standard of excellence required by the Board of Trustees. In 1960, five Queen Elizabeth Fellowships were awarded, and at its annual meeting in Ottawa in March of this year, the Board of Trustees appointed three additional Fellows.

Queen Elizabeth Scientists are chosen from more senior personnel who are prepared to devote their careers to pediatric research. To assist in their support the Fund will provide to any university with a candidate selected for this award, the sum of $10,000 annually for three years and $5000 per year for an additional three years, provided that the university concerned will continue to employ such personnel thereafter and will provide them with suitable accommodation and laboratory and other facilities required in the conduct of their research.

By these means the Trustees of the Queen Elizabeth Fund are attempting to use the Fund's resources to stimulate and encourage the recruitment and training of Canadian scientific workers of a high standard of excellence in the field of children's diseases. The urgent need for this development is emphasized by the fact that Canadian pediatric research lags far in arrears of that being conducted in the United Kingdom and the United States, a state of affairs reflected in Canada's high infant mortality rate which ranks but thirteenth according to world statistics, despite the relatively high level of this country's economy and living standards.

In view of the stringent requirements demanded of candidates by the Fund's Board of Trustees, awards to date have been granted to only a fraction of those who have made application. Consequently the income from the initial $1,000,000 fund has been adequate to meet immediate needs. The Trustees are, however, fully cognizant of the natural history of such funds and recognize that, as knowledge of the availability of this source of support becomes more widespread, an increasing number of highly qualified candidates will likely submit applications for assistance, in which event the limited sum now available for distribution would soon become inadequate.

It is the hope of the Fund's administrators that on subsequent visits of members of the Royal Family to Canada, federal, provincial and possibly certain municipal governments will see fit to honour

Her Majesty by making additional contributions to the Queen Elizabeth II Fund. The Trustees are aware, however, of the necessity of exploring other sources of revenue. Although it is not planned that such explorations would involve the canvassing of physicians, it is of considerable importance to those charged with the pursuit of the Fund's objectives that the doctors of Canada be familiar with its background and its program of activities. In conjunction with the Canadian Bar Association, ways and means are being sought whereby lawyers and trust companies may be fully informed concerning the Fund in order that they may provide such information to clients consulting them with a view to arranging bequests for such purposes. It is natural that any individual contemplating such a bequest would seek his doctor's advice, in which event the physician's familiarity with the Fund and the activities which it sponsors assume obvious importance.

THE T. G. H. DRAKE PEDIATRIC COLLECTION

LIBRARY and historical night at the Toronto Academy of Medicine on April 11 was the occasion for the official opening of one of the world's finest private collections of pediatric literature, art, instruments and utensils, now on permanent display in the foyer of the Academy's Osler Hall and library. This treasure trove of some 1500 rare books and more than 3000 specimens, acquired by the late Dr. T. G. H. Drake during the thirty-five years of his association with the Toronto Hospital for Sick Children, was bequeathed, on his death in 1959, to the Toronto Academy.

The 1500 priceless volumes, a saga of mankind's learning and art representing the best in medical literature on the care of children, constitute a monument to Dr. Drake as a medical bibliophile in the most exact sense of the term. Among them may be found the 1487 edition of the first book devoted to the subject of pediatrics, the "Libellus de Egritudinibus Infantium" by Paulus Bagellardus; Metlinger's "Ein Regiment der Jungen Kinder" (1473), the first pediatric text to be written in the vernacular; a copy of the life of St. Margaret, patron saint of pregnant women, printed in 1500, and according to popular custom laid upon the abdomen of expectant mothers during delivery. The five editions of Thomas Phaire's "Boke of Chyldren" (1546) represent the earliest pediatric text published by an English author. John Browne's "Adenochoiradelogia" (1684) presents an intriguing contemporary account of the curious rite of "touching for the King's Evil" as practised by the Stuart Kings. The "Countesse of Lincolne's Nursurie" (1622) was written with the purpose of urging mothers of all classes to nurse their children, a forerunner, no doubt, of the message preached with such eloquent evangelistic fervor by Dr. Drake's late chief.

A collection of Egyptian, Greek and Roman articles, *circa* 1000 B.C.-100 A.D., includes surgical and cosmetic instruments, children's jewelry, oil lamps, feeding vessels and replicas of gods and goddesses of children, maternity and fertility. Isis, goddess of maternity, her husband, Osiris, and son Horus are depicted in various-sized figures. Horus, who presumably suffered from a birth injury with residual weakness of his legs, is always shown in a sitting position. Other rare items from this period are feeding vessels in the shape of a cow and a mouse, a jointed pottery doll *circa* 400 B.C., and oil lamps with the outline of a frog that were thought to be of special value in the lying-in room.

An impressive display of 18th and 19th century pottery and porcelain from the factories of Chelsea, Bow, Spode, Staffordshire, Lowestoft, Derby, Niderviller and Capo di Monte includes such items as pap warmers, pap boats, feeding bottles, barber-surgeons' bleeding bowls, drug jars and figures of nursing mothers and wet nurses in action.

The collection of silver from the 17th to 19th century features such articles as pomanders, vinaigrettes, spouted feeders, a Commonwealth bleeding bowl, lancet cases, tongue scrapers, christening mugs, medicine spoons and rattles, all of which provide a fascinating glimpse of pediatric practices of their era. The pomanders and vinaigrettes are small, beautifully crafted containers for mixtures of aromatic substances "for the prevention of ill airs or scents" and supposedly anti-infective materials. The tongue scrapers were as common a necessity for 18th century toilet as today's tooth brush. By their use "the fur and slime may be removed which is often a comfort to the invalid."

Classic 18th century pewter utensils are exemplified by the spouted infant feeders, enema and urethral syringes, bleeding bowls and bed pans of impressive and sometimes rather startling and formidable design.

Another fascinating feature of the collection is the gallery of medical caricatures by the Cruikshanks, Gilbray and Rowlandson which unveil a panorama of "medicine, its evolution, its discoveries and its failures from the standpoint of the patient . . ."

Prints, documents and laws pertaining to wet-nursing in England and France during the 18th century; coins, medals and tokens used in the ceremony of "touching for the King's Evil", many of them depicting Apollo slaying the dragon of disease; a collection of stamps issued in support of charities concerned with health, widows and orphans, child welfare and Boy Scouts; a roomful of 17th century children's furniture, fine examples of the art of the turner and joiner; and an array of mortars and pestles from the 15th to 18th centuries: all add to the wealth of treasures in the Drake Collection which will surely make the Toronto Academy of Medicine a veritable Mecca for afficionados of the history, art and culture of medicine in general, and pediatrics in particular.

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LETTER TO THE EDITOR

THE MEDICAL LETTER ON DRUGS AND THERAPEUTICS

To the Editor:

The Canadian Medical Association Journal has generously provided space in its correspondence columns for a discussion by two Canadian physicians of the pros and cons of The Medical Letter on Drugs and Therapeutics (*Canad. M. A. J.*, 84: 439, 1961; 84: 737, 1961), and I hope that as one of the editors of *The Medical Letter*, I may be allowed space for a further comment.

In the April 1 issue of the *Journal*, Dr. M. A. Ogryzlo questions the worth of such a service as that provided by *The Medical Letter*, saying, ". . . a small editorial staff is not likely to be well versed in the therapeutic value of all newly introduced therapeutic agents." The implication that *The Medical Letter* relies solely on the knowledge of its editorial staff in appraising drugs indicates a lack of awareness of the special purpose and the method of operation of this non-profit publication.

The Medical Letter is unique among medical periodicals in that its appraisals never present the views of one person or of a single small group of editors or investigators. The distinguished Advisory Board of our publication is not window-dressing. A preliminary draft of every drug appraisal prepared for *The Medical Letter*, no matter how eminent the original writer, is reviewed by every member of both the Editorial and the Advisory Boards, and the reviewed copies are returned with their questions and criticisms. The preliminary drafts are also sent for critical review to investigators who have had special clinical and experimental experience with the drugs or the types of drugs being reviewed. At the same time, copies are mailed to the medical directors of the pharmaceutical companies whose drugs are being appraised; and despite inevitable disagreement on some points, almost all have made constructive criticisms and suggestions which have added to the usefulness of the material. The appraisals are revised and re-revised on the basis of such reviews and as the result of ensuing correspondence and telephone discussions. If, as occasionally happens, the differences among consultants are such as to defy resolution, the effort to appraise the drug is dropped, sometimes after many months of work.

Unlike other medical periodicals, whose proper function it is to present studies or opinions—often conflicting—of different writers, *The Medical Letter* offers the pooled judgment of a large, competent and unbiased group of investigators and clinicians. More than 200 clinicians and investigators have participated in the preparation and active review of *Medical Letter* drug appraisals during the brief period of its existence, and the list continues to grow.

Dr. Ogryzlo is disturbed by the fact that *The Medical Letter* is not free of error, and he points to one unquestionable error and to one incidental statement in an area where facts are few and on which expert opinion differs. It is true that, despite all our care, we have indeed made errors (and corrected them), and without doubt there will be errors in the future. If complete freedom from error were to be the criterion for acceptance or rejection of a medical publication, I am afraid that the shelves and racks of our medical libraries would be quite bare. Unfortunately, no medical editor has yet found a way to eliminate errors completely (such as the error of transcription which resulted in the incorrect dosage figure for colchicine).

The basic question raised by Dr. Ogryzlo relates to ". . . the difficulty in obtaining authentic information concerning the therapeutic value of drugs . . ." Obviously, the practising physician cannot do more than a very small part of the study of reports of clinical trials and the consultation with experts that would be required for intelligent selection and use of new therapeutic agents. In this dilemma, should he turn to the drug advertisements and the detail men, or to the large body of unbiased consultants whose views are presented through *The Medical Letter*? We are pleased that a steadily growing number of physicians (some 1500 of them in Canada) make the latter choice. We are also pleased that despite all the hazards of judgment in a field in which there are no absolutes and many differences in findings and opinions, remarkably few of the judgments of therapeutic value expressed since the first issue of *The Medical Letter* appeared in January 1959 have required revision on the basis of subsequent evidence.

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PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

LUNENBURG-QUEENS MEDICAL SOCIETY

The regular midwinter session of the Lunenburg-Queens Medical Society was held at Lunenburg, Wednesday, February 22.

Two new members were elected, Dr. Gordon MacLellan, of Mahone, and Dr. Lawrence Braine, of Chester. Action was taken on resolutions passed by the Valley Medical Society at the regular meeting January 31. These resolutions had to do with the management of the Victoria General Hospital, and fees for expert evidence by medical men. Dr. W. N. Rehfuss, of Bridgewater, then read a paper on "Personal Experiences with the Various Vaccines". The concluding paper was "Three Hours in Trudeauville" by Dr. L. T. W. Penney, of Lunenburg.

In the evening, Dr. A. F. Miller, superintendent of the Provincial Sanatorium, Kentville, read a paper on "Tuberculin, its Diagnostic and Therapeutic Value in Tuberculosis". This paper was fully discussed, and many ideas were exchanged as to the proper steps to be taken in order to arrest the progress of tuberculosis in Nova Scotia. It was unanimously agreed that much more might be accomplished, and that although the government of Nova Scotia was to be commended for what it had already done, the sanatorium at Kentville is inadequate and must be enlarged. A deputation, consisting of Dr. W. N. Cochran, of Mahone, Drs. Rehfuss and Churchill, of Bridgewater, Dr. W. H. Macdonald, of Rose Bay, and Dr. L. T. W. Penney, of Lunenburg, was appointed to confer with the other provincial medical societies to draw up a suitable memorial, and, in conjunction with the representatives of those other societies, to wait upon the government at Halifax, and urge the necessity of improvements and alterations.—*Canadian Medical Association Journal*, 1: 388, April 1911.

THE LONDON LETTER

A Day in the Hospital

Few of us who have been patients in hospital would disagree with the thesis that the patient's day is all too long, beginning in most British hospitals at 6 a.m. and continuing with noise and bustle far into the evening. A group of British nurses were asked to look into this matter and have recently published, under the auspices of the Central Health Services Council, a report, "The pattern of the in-patient's day". One of the traditional arguments for starting the day at such an ungodly hour is that the ward must be shipshape for the doctors' visits, but it is surely time that the remnants of the feudal system disappeared and that doctors were occasionally allowed to see their patients in a state of untidiness.

The timetable given by the committee in their report shows a period of activity going on from 6 a.m. to 10 p.m., with feverish rushes between 6 a.m. and noon, at a time when some patients do not view disturbance with pleasure. The nurses have been caustic about some of the rituals which survive in British hospital practice, such as the morning recording of temperatures, pulse rate and respiration rate, the incessant bedmaking, and the so-called sanitary round with bedpans and bottles. It is also still axiomatic that the higher ranks of the medical staff must not see anyone at work in the ward when they visit, and it is suggested that a little flexibility here and also in staggering visiting hours by relatives would help to cut down the period of activity.

Memorial to Fleming

In mid-March a new fund for research in Britain was launched in London, to be called the Fleming Memorial Fund for Medical Research, in memory of the late Sir Alexander Fleming. The target for the fund is one million pounds, and a star-studded list of patrons, trustees and councillors support the project, including the Queen Mother, the Prime Minister, the Archbishop of Canterbury and Sir Howard Florey. The appeal is international and the money will be used to advance and expand basic medical research designed to elucidate the causes of disease and assist in their prevention and cure. It is unnecessary to add that there is not nearly enough money presently available for basic research and that anyone considering supporting medical research would do well to look into the claims of this worthy new cause.

Staffing of Hospitals

Widespread dissatisfaction with the staffing of hospitals in the United Kingdom has been based on a few obvious defects. One is the almost total divorce in many areas of the general practitioner from the life of the local hospital under the National Health Service structure, and another is the unfortunate position of the redundant registrar. The registrar category was originally intended for specialists in training and was never intended to be a career appointment, yet the relative plethora of registrars and the relative scarcity of appointments in the next grade up—that of consultant—has meant that many of these men continue to serve for years at the same level, unless their patience becomes exhausted and they emigrate to places like Canada.

Nearly three years ago, a working party was appointed by government to look into the whole question of hospital staffing, and the party has now reported its findings. It was a joint committee culled from organized medicine and government and chaired by Sir Robert Platt, and it has not concealed its critical feelings, since it says early in the report: ". . . there is a noteworthy absence of testimony that the present structure [of hospital staffing] has proved satisfactory in all respects, or is the best that can be devised." As regards general practitioners, the report suggests that suitably experienced ones should be given part-time hospital appointments on a regular daily visiting basis as well as clinical assistantships in special clinics. However, the working party insists that the consultant should be the only doctor taking full personal responsibility for hospital patients, and that there is at present a deficit in this grade. To absorb some of those aspirants to consultant rank who have been unable to climb higher, the report proposes a new grade of "medical assistant" with unlimited tenure of appointment, to encourage younger doctors to remain in the hospital service longer; some of the medical assistant posts can be given to part-time general practitioners. The rank of the medical assistant would be between those of registrar and consultant.

The working party did not think that the staffing in casualty departments was satisfactory, and urged closer supervision by consultants. It was also alarmed that work properly belonging to consultants was being discharged by personnel in junior grades. It is of course no secret that the junior grades of most hospitals in Britain are filled by recruitment of foreign graduates, and the report shows that the percentage of junior hospital staff not born in the U.K. varies from 50% in the north of England to 11% in parts of Scotland. The committee thinks that the problem of junior staffing will not be solved until young doctors can be persuaded to serve longer and certain gaps are filled by general practitioners. The *British Medical Journal* in a leader expresses the hope that study of the report may lead to a plan which "will be an imaginative one and not merely aimed at papering over cracks in the structure."

Trouble for Motoring Sinners

Great Britain has for some time been more lenient than either the U.S.A. or the Scandinavian countries in dealing with motorists under the influence of alcohol or drugs. Now the government proposes to establish stiff penalties for drivers caught in this state. For the first time, analyses of blood, urine or breath for alcohol or drugs may be allowed to help the courts in assessing the fitness of drivers, though such tests are not made compulsory. Moreover, refusal of consent to the taking of or provision of a specimen for analysis may be treated as supporting evidence on behalf of the prosecution or as rebutting defence evidence. The breathalyser will be used, although it is believed that it does not yet come up to the standard desirable in Britain. The British Standards Institute will set up a

standard for the instrument to which manufacturers will have to conform. Analyses will not be made unless there is some evidence that a driver is unfit to drive. Penalties will also be stiffened for driving under the influence of drink or drugs, and a conviction will automatically disqualify for 12 months, and, if repeated within 10 years, for another three years. In addition, fines are to be doubled for this type of offence, as for some others such as speeding or ignoring pedestrian crossings.

BLOOD TESTS FOR PATERNITY

A Bill has recently been introduced into the House of Lords to make it compulsory in cases of disputed paternity for the accused man and the complaining woman to undergo blood tests. At present, there are about 5000 applications annually for affiliation orders against men alleged to be the father of children born to unwed mothers, and only about 200 of these cases involve voluntary blood tests. It would seem that many decisions must, in these circumstances, be based on the "clinical impression" rather than scientific evaluation. Yet curiously enough, when the Bill was introduced, one of the medical members of the House, Dr. Summerskill, spoke against it on the ground that it would inflict hardship on the girls concerned, while another member said that it was often a matter of good fortune rather than good management whether a particular man was the father or not. On the other hand, Lord Taylor (also a medical member) thought that such tests would go far towards eliminating the 50 to 60 miscarriages of justice occurring annually because they were not applied. It seems however that government is not entirely happy about the Bill, mainly on the grounds of the expense involved to secure a small percentage of helpful results. S. S. B. GILDER

MEDICAL NEWS IN BRIEF

VIRAL INFECTION AND SUDDEN DEATH IN INFANTS

An attempt was made to isolate viral agents from tissues obtained at autopsy from 48 infants whose deaths were sudden and unexpected and from two who met traumatic deaths.

Viral agents were detected by Gold *et al.* (*New England J. Med.*, 264: 53, 1961) in specimens obtained from 12 subjects. In five, the agent was isolated from stool or pharynx, and in seven additional cases from central nervous system tissues. All agents were members of the enterovirus family.

This study suggests a relation between viral infection and sudden death in infants, and also points out the need for further study.

THE DOCTOR'S PLACE IN THE PATIENT'S HOSPITAL

Recently a paper with this title, written by Dr. S. T. Hayward, a consultant psychiatrist, appeared in the *Lancet* (1: 387, 1961).

The theme of Dr. Hayward's presentation is that hospitals exist for the benefit of patients; they do not exist in order to glorify hospital boards, or to provide comfortable employment for various varieties of administrators. Similarly, the doctor's primary function is to care for, and to understand, patients.

If the doctor's ego is bruised by his inability to cure the patient, he should not retaliate, either by rejecting the patient or by punishing him by doing a leukotomy or some other similarly vigorous form of treatment. In the doctor-patient relationship the doctor's emotional need is fulfilled by recovery of the patient. In psychiatry, especially, the doctor should be at ease with his own omnipotence fantasies.

There is a need for a team approach in mental hospitals, and indeed in all hospitals. This does not refer to an amorphous team, with no direction, permeated with well-meaning but fuzzy "togetherness". The team should be led by the doctor, and all nurses, social workers, occupational therapists, and others involved in patient care, should lose their narrow professionalism and co-operate for one purpose only, and that is the welfare of the patient, whether the patient can be cured or not.

PLEUROPULMONARY MANIFESTATIONS OF SYSTEMIC LUPUS ERYTHEMATOSUS

The pleuropulmonary features of systemic lupus erythematosus are among the most frequent of the visceral manifestations of this disease. Forty-eight cases are reviewed by Alarcon-Segovia and Alarcon (*Dis. Chest*, 39: 7, 1961), in which the diagnosis was proved by a positive L.E. cell test, or various histological studies or both, including 19 autopsies. The clinical, radiological and pathological features of the pleuropulmonary manifestations are discussed. The lungs were affected in 79% of cases; this percentage was surpassed only by that for renal involvement. Although respiratory symptoms and important radiological changes were common, physical findings were usually scarce. Three fundamental radiological patterns were found in the pulmonary parenchyma; in seven cases there was a fine micronodular infiltrate; in another seven a diffuse infiltrate resembling pneumonitis, and in four, linear shadows of atelectasis. The main characteristic of these findings is the changing pattern, which is illustrated and discussed. Hydrothorax was found by chest radiographs in 22 cases and was of sufficient degree to be detected by physical examination in half of these. The pathological data at autopsy were nonspecific, and in spite of important clinical and radiological findings, usually little was found post mortem. Specific lesions were found in the lungs in only three cases.

(Continued on advertising page 30)

PROGRAM

FOR THE

94th ANNUAL MEETING

OF

The Canadian Medical Association

MONTREAL, QUEBEC

June 19 - 23, 1961

The 94th Annual Meeting of The Canadian Medical Association will be held at Montreal, Quebec, Monday, June 19 through Friday, June 23, 1961. Convention headquarters will be The Queen Elizabeth Hotel. The timetable of the scientific sessions and social events will be as follows:

Monday, June 19 Tuesday, June 20 Wednesday (morning only), June 21	Meeting of The General Council
Monday, June 19	12.30 p.m.—Luncheon for Members of The General Council 6.00 - 8.00 p.m.—Wine-Tasting Supper Party, Montreal Museum of Fine Arts
Tuesday, June 20	9.00 a.m. - 5.00 p.m.—Scientific Sessions 6.30 p.m.—Dinner to The General Council
Wednesday, June 21	9.00 a.m. - 5.00 p.m.—Scientific Sessions. 12.30 p.m.—Luncheon and Annual Business Meeting of the Quebec Division 8.15 p.m.—The Annual General Meeting President's reception and dance
Thursday, June 22	9.00 a.m. - 5.00 p.m.—Scientific Sessions Golf Tournament in afternoon 6.00 p.m.—Civic Reception at The Chalet on Mount Royal
Friday, June 23	9.00 a.m. - 5.00 p.m.—Program on Medical Economics

A feature of the meeting this year will be a showing of medical films Tuesday through Thursday and a number of Scientific Exhibits.

SCIENTIFIC PROGRAM

Tuesday, June 20

TEACHING SESSIONS

9.00 - 10.30 a.m. — Marquette Room

Some Interesting Aspects of Endocrinology and Nutrition

Chairman:
DR. D. R. WILSON, Edmonton

Participants:
DR. P. B. ROSE, Edmonton
DR. CHARLES HOLLENBURG, Montreal
DR. JACQUES DUCHARME, Montreal

9.00 - 10.30 a.m. — Jolliet Room

The Acute Abdomen

Chairman:
DR. A. D. MCKENZIE, Vancouver

Participants:
DR. J. G. HOWLETT, Montreal
DR. R. A. H. KINCH, London
DR. J. R. F. MILLS, Toronto
DR. L. MORISSETTE, Montreal

10.45 a.m. - 12.15 p.m. — Marquette Room

The Recognition and Office Management of Minor Psychiatric Disorders

Chairman:
DR. GORDON A. COPPING, Montreal

Participants:
DR. K. A. YONGE, Edmonton
DR. P. G. EDGELL, Montreal
DR. H. E. LEHMANN, Montreal
DR. FRANÇOIS CLOUTIER, Montreal

10.45 a.m. - 12.15 p.m. — Jolliet Room

Practical Problems in Intravenous Supportive Therapy

Chairman:
DR. FRASER N. GURD, Montreal

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Participants:
DR. R. A. MACBETH, Edmonton
DR. JOHN C. BECK, Montreal
DR. EUDORE SAVOIE, Montreal

2.00 - 3.30 p.m. Marquette Room

Prenatal Care

Chairman:
DR. B. D. BEST, Winnipeg

Participants:
DR. W. R. FOOTE, Montreal
DR. F. J. TWEEDIE, Montreal
DR. P. A. RECHNITZER, London
DR. O. A. SCHMIDT, Winnipeg

2.00 - 3.30 p.m. Jolliet Room

Hypertension — Atherosclerosis

Chairman:
DR. JACQUES GENEST, Montreal

Participants:
DR. LOUIS HORLICK, Saskatoon
DR. JOHN A. LEWIS, London
DR. W. FORD CONNELL, Kingston
DR. JOHN D. MORROW, Toronto
DR. A. E. THOMSON, Winnipeg

SECTION OF GASTROENTEROLOGY

9.00 a.m. - 12.00 noon Peribonca Room

Chairman: DR. R. D. MCKENNA, Montreal
Business Meeting

2.00 - 3.15 p.m. Peribonca Room

The Diagnosis and Management of Hiatus Hernia and Esophagitis

Chairman:
DR. R. C. DICKSON, Halifax

Participants:
DR. R. G. FRASER, Montreal
DR. D. D. MUNRO, Montreal
DR. C. M. BALLEM, Montreal

3.30 - 5.00 p.m. Peribonca Room

Evaluation of Current Diagnostic Methods in Diseases of the Digestive Tract

Chairman:
DR. A. BOGOCH, Vancouver

Participants:
Evaluation of Tele-Roentgen Studies of the Digestive Tract
DR. A. JUTRAS, Montreal
Esophageal Acid Perfusion Test and Motility Studies
DR. J. SIDOROV, Halifax
Esophagoscopy and Gastroscopy
DR. P. LETENDRE, Montreal
Tests of Intestinal Absorption
DR. J. M. FINLAY, Toronto
The Value of Peroral Small Bowel Biopsy
DR. D. J. BUCHAN, Saskatoon
Liver Biopsy Using the Menghine Needle
DR. P. M. O'SULLIVAN, Toronto

Wednesday, June 21

TEACHING SESSIONS

9.00 - 10.30 a.m. Marquette Room

The Value of Anticoagulant Therapy

Chairman:
DR. K. J. R. WIGHTMAN, Toronto

Canadian Government Travel Bureau, Ottawa

Montreal—from the lookout atop Mount Royal.

Participants:
DR. PAUL DAVID, Montreal
DR. H. J. M. BARNETT, Toronto
DR. LOUIS HORLICK, Saskatoon

9.00 - 10.30 a.m. Jolliet Room

The Management of Peripheral Venous Thrombosis

Chairman:
DR. JAMES A. KEY, Toronto

Participants:
DR. J. C. LUKE, Montreal
DR. T. S. PERRETT, Vancouver
DR. K. W. G. BROWN, Toronto
DR. J. G. QUENNEVILLE, Montreal
DR. D. R. WILSON, Toronto

9.00 - 10.30 a.m. Duluth Room

The Significance and Management of Rectal Bleeding

Chairman:
DR. IAN MACKENZIE, Halifax

Participants:
DR. R. A. MUSTARD, Toronto
DR. JACQUES BRUNEAU, Montreal
DR. IVAN T. BECK, Montreal
DR. ARNOLD ROGERS, Winnipeg
DR. CHARLES BIRO, Saskatoon

10.45 a.m. - 12.15 p.m. Marquette Room

Chronic Respiratory Disease, Its Diagnosis and Management

Chairman:
DR. RONALD V. CHRISTIE, Montreal

Participants:
DR. D. V. BATES, Montreal
DR. J. A. P. PARE, Montreal
DR. R. G. FRASER, Montreal

10.45 a.m. - 12.15 p.m. Duluth Room

The Early Management of Injuries

Chairman:
DR. W. MASON COUPER, Montreal

Participants:
DR. G. G. P. BERTRAND, Montreal
DR. E. B. TOVEE, Toronto
DR. D. D. MUNRO, Montreal
DR. G. F. PENNAL, Toronto

Montreal Tourist and Convention Bureau

The Province of Quebec Handicraft Centre (a ten-minute bus ride from the Queen Elizabeth Hotel).

10.45 a.m. - 12.15 p.m. Jolliet Room

Allergy and Collagen Diseases

Chairman:
DR. JACQUES LEGER, Montreal

Participants:
DR. BRAM ROSE, Montreal
DR. R. H. MORE, Kingston
DR. L. MORISSETTE, Montreal
DR. L. G. JOHNSON, Montreal

GENERAL SESSION

Chairman: DR. R. MACGREGOR PARSONS, Red Deer

2.30 - 3.30 p.m. The Grand Ballroom

The Swing of the Pendulum
DR. D. EWEN CAMERON, Montreal

The Effect of X-Ray Radiation on the Embryo-Fetus
DR. MAURICE MAYER, Paris, France

TEACHING SESSIONS

3.30 - 5.00 p.m. The Grand Ballroom

The Management of Urinary Infection

Chairman:
DR. JAMES M. CAMPBELL, Saskatoon

Participants:
DR. DOUGLAS G. CAMERON, Montreal
DR. HARRY MEDOVY, Winnipeg
DR. ROBERT D. JEFFS, Toronto

3.30 - 5.00 p.m. Marquette Room

Deafness, Its Diagnosis and Management

Chairman:
DR. FERNAND MONTREUIL, Montreal

Participants:
DR. W. ALEXANDER, Winnipeg
DR. B. W. TANTON, Vancouver
DR. K. MCASKILE, Toronto
DR. H. E. MCHUGH, Montreal
DR. PAUL ROBERT, Montreal

Thursday, June 22

CASE ANALYSIS CLINIC

9.00 - 10.30 a.m. The Grand Ballroom

Chairman:
DR. H. ROCKE ROBERTSON, Montreal

Participants:
DR. A. D. MCKENZIE, Vancouver
DR. R. C. HARRISON, Edmonton
DR. J. C. LUKE, Montreal

CLINICO-PATHOLOGICAL CONFERENCE

9.00 - 10.30 a.m. Marquette Room

Two Cases for Diagnosis and Discussion (see page 1089)

Chairman:
DR. DOUGLAS G. CAMERON, Montreal

Participants:

Pathologists
DR. G. C. MCMILLAN, Montreal
DR. CARLTON AUGER, Quebec

Clinicians
DR. C. C. GRAY, Toronto
DR. R. C. DICKSON, Halifax
DR. J. M. KILGOUR, Winnipeg
DR. J. G. HOWLETT, Montreal

TEACHING SESSION

9.00 - 10.30 a.m. Jolliet Room

Emergencies in the Newborn

Chairman:
DR. HARRY MEDOVY, Winnipeg

Participants:
DR. CLINTON A. STEPHENS, Toronto
DR. R. A. USHER, Montreal
DR. JOHN M. BOWMAN, Winnipeg

GENERAL SESSION

Chairman: DR. G. W. HALPENNY, Montreal

11.00 a.m. - 12.15 p.m. The Grand Ballroom

The Lister Lecture: Biliary Surgery in Sweden
DR. HUGO ROSENQVIST, Stockholm, Sweden

The Medical Research Council
DR. R. F. FARQUHARSON, Toronto

Chairman: DR. H. S. MORTON, Montreal

2.30 - 3.30 p.m. The Grand Ballroom

Iatrogenic Hazards in Anesthesia
DR. LEROY D. VANDAM, Boston

Transient Cerebral Ischemia
DR. CHARLES M. FISHER, Boston

TEACHING SESSIONS

3.30 - 5.00 p.m. The Grand Ballroom

New Concepts of Infectious Diseases of Childhood

Chairman:
DR. JULES CHARBONNEAU, Montreal

Participants:
DR. A. R. FOLEY, Quebec
DR. VICTOR MARCHESSAULT, Montreal
DR. VYTAUTAS PAVILANIS, Montreal
DR. CRAWFORD S. ANGLIN, Toronto

3.30 - 5.00 p.m. Duluth Room

Dysmenorrhea

Co-Chairmen:
DR. GEORGE B. MAUGHAN, Montreal
DR. PIERRE MEUNIER, Montreal

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Participants:
DR. ELINOR F. E. BLACK, Winnipeg
DR. PAUL DUMAS, Montreal
DR. JOHN S. HENRY, JR., Montreal
DR. E. H. SHABANAH, Montreal

3.30 - 5.00 p.m. Mackenzie Room

Radiation Protection in Diagnostic Radiology and in Industry

Chairman:
DR. D. L. MCRAE, Montreal

Participants:
DR. R. C. BURR, Kingston
DR. ALBERT JUTRAS, Montreal
DR. F. D. SOWBY, Ottawa
DR. C. G. STEWART, Chalk River

Friday, June 23

PROGRAM ON MEDICAL ECONOMICS

Chairman: DR. J. A. MCMILLAN, Charlottetown

9.00 - 10.30 a.m. The Grand Ballroom

The Effect of Universal Hospital Insurance on Medical Practice

Chairman:
DR. JOSEPH A. MACDOUGALL, Saint John

Participants:
DR. R. W. I. URQUHART, Toronto
DR. J. G. TURNER, Montreal
DR. R. F. MALO, Ottawa
DR. J. P. MCINERNEY, Saint John

10.45 a.m. - 12.15 p.m. The Grand Ballroom

Government and Medicine
DR. WILDER G. PENFIELD, Montreal

Health Insurance in Australia
DR. T. J. QUINTIN, Sherbrooke

Health Insurance in Sweden
DR. HUGO ROSENQVIST, Stockholm, Sweden

"La Poudrière" (The Powder House), an international theatre located on St. Helen's Island, Montreal.

2.30 - 5.00 p.m. The Grand Ballroom

The Role of the Royal Commission on Health Services
HONOURABLE EMMETT M. HALL, Regina

Existing Deficiencies in Health Services—The Saskatchewan Experience
DR. H. D. DALGLEISH, Saskatoon

A Practical Approach to Medical Insurance for Canadians

Chairman:
DR. G. E. WODEHOUSE, Toronto

Participants:
DR. J. A. MCMILLAN, Charlottetown
DR. L. R. RABSON, Winnipeg
DR. D. F. MCPHERSON, Lethbridge
DR. E. C. MCCOY, Vancouver

THE SOCIAL PROGRAM

The Planning Committees in Montreal have arranged a number of interesting social events, which will commence on Monday evening, June 19, when members and their wives will participate in a wine-tasting supper party. This event will take place in the Museum of Fine Arts, and those present will have the opportunity of tasting some twelve different imported wines accompanied by a similar number of cheeses. The meal will be rounded out with special hors d'oeuvres and pastries. On Tuesday evening, the Annual Dinner to The General Council will take place in the Ballroom of the Queen Elizabeth Hotel, and special musical entertainment has been arranged for this occasion. All are invited.

The highlight of our convention week will be the Annual General Meeting, which will commence at 8.15 p.m. on Wednesday, June 21. At this time the colourful ceremony of the installation of the President will take place, and His Excellency Major-General Georges P. Vanier, D.S.O., M.C., C.D., Governor General of Canada, will be made an honorary member of the C.M.A. It is interesting to note that this is only the third time in the history of the C.M.A. that a non-medical person has been awarded this honour. The other two honorary memberships were presented to the Right Honourable Vincent Massey, former Governor General of Canada; and His Royal Highness The Prince Philip, Duke of Edinburgh. In addition to the above, the Canadian Medical Association will honour its Senior Members who have been nominated by their respective Divisions.

THE NINETY-FOURTH ANNUAL MEETING: PROTOCOLS OF CASES TO BE DISCUSSED AT THE CLINICO-PATHOLOGICAL CONFERENCE, JUNE 22

The two case summaries reproduced below will be the subjects of discussion at a Clinico-Pathological Conference which will be held on Thursday, June 22, during the Association's Annual Meeting. Dr. Douglas G. Cameron, Montreal, will be Chairman of the Conference and the other participants will be: Dr. Gardner C. McMillan, Montreal, and Dr. Carlton Auger, Quebec City, pathologists; Dr. C. C. Gray, Toronto, Dr. R. C. Dickson, Halifax, Dr. John Kilgour, Winnipeg, and Dr. John Howlett, Montreal, clinicians.

Members of the Association who are planning to attend the Annual Meeting are invited to study these protocols at their leisure at home, to provide added interest in their discussion at the Clinico-Pathological Conference and to derive the maximum instructional benefit from this session.

CASE 1

A 64-YEAR-OLD white man developed a rash on his left leg following trauma in October 1960. The rash failed to clear completely and three months later it spread to the trunk and other limbs.

FIRST ADMISSION

On January 4, 1961, he was admitted to hospital complaining of the itchy skin eruption. The only previous illness of note was gout which began in his great toe three years before and later involved his left knee. This condition was treated with colchicine alone for two years and with colchicine and phenylbutazone (Butazolidin) during the third year. Both agents were discontinued three weeks before admission. His mother died of asthma at 56 years and his father of cancer at 71. One brother died of high blood pressure.

The patient's temperature was 99.4° F., pulse 70, and blood pressure 150/95 mm. Hg. The rash was noted to involve all limbs and the front of the trunk. It was maculopapular, confluent and did not weep. The lungs were clear and the heart was normal. His weight was steady at 195 lb. The joints were not deformed, but there was a trace of pretibial edema. Urine specific gravity ranged up to 1.017, and one sample taken while the patient was febrile contained a trace of protein, and 5-8 red blood cells per high-power field. The blood urea nitrogen (BUN) value was 21 mg. %. The dermatitis subsided slowly on starch baths, milk and water compresses. On the third hospital day he developed acute gout in his right big toe which responded promptly to administration of ACTH and probenecid (Benemid). Maintenance doses of colchicine and probenecid were prescribed and the patient was sent home on January 21 free of symptoms.

SECOND ADMISSION

He was re-admitted on February 22, 1961, because of severe dyspnea, edema and oliguria. He had been well until two weeks before admission when he developed a sore throat and cough with scanty sputum, occasionally blood-streaked. The urine decreased in amount and became "tea-coloured". He had anorexia and mild diarrhea. Colchicine and probenecid were discontinued. Ten days before admission, edema, puffiness of the eyes and headache appeared. At the time of admission dyspnea was severe and he had gained 15 lb. in weight.

On examination, his temperature was 100° F., pulse 108, respirations 28, and blood pressure 130/80. He was in respiratory distress but there was no cyanosis. The pharynx was diffusely red. The pulse was regular, the heart was not enlarged, the sounds were clear, but a gallop rhythm was heard. There was dullness to percussion at the lung bases and moist rales were heard throughout both lung fields. There was pitting edema of the ankles but no jugular venous engorgement. The skin was clear. Twitching movements of the extremities, lethargic speech and drowsiness were noted. Urine passed at this time was deeply coloured and contained 300 mg. % protein; microscopic examination was not done. Non-protein nitrogen value was 70 mg. %.

The clinical picture of uremia prompted his transfer to The Montreal General Hospital on February 25, 1961.

THIRD ADMISSION

The clinical picture was much the same. His temperature was 99.6° F., pulse 100, respiratory rate 26, and blood pressure 150/85. He weighed 203 lb. There were no retinal hemorrhages and no papilledema, but a patch of retinal exudate was seen. Moist rales were heard at the lung bases and signs of bilateral pleural effusion were noted. There was shifting dullness in the abdomen.

Urine obtained on admission (an insufficient amount for determination of the specific gravity) was "coffee-coloured" and contained 300 mg. % protein and gross numbers of red cells, as well as hyaline, granular and red cell casts. Results of determination of serum values on admission showed BUN 69 mg. %, chloride 89 mEq./l., bicarbonate 21 mEq./l., sodium 118 mEq./l., and potassium 6.7 mEq./l. The blood picture was as follows: Hb. 10.7 g., hematocrit 33%, sedimentation rate 33 mm. in one hour, reticulocytes 1%, white cell count 12,100, with 86% polymorphonuclear leukocytes, 4% lymphocytes and 6% monocytes. An electrocardiogram showed sinus tachycardia. A chest roentgenogram revealed small bilateral pleural effusions, pulmonary congestion, and a heart shadow within normal limits. A plain film of the abdomen showed normal kidney outlines but no opacity suggesting stones.

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An inferior vena cava catheter was introduced and fluid intake was restricted to 400 c.c. per day together with an amount equivalent to the daily urine output. The daily weight was recorded, he was digitalized, exchange resins were administered and he was given anabolic hormone therapy. During the first eight days his urine output varied from 50 to 300 c.c. per 24 hours. His weight dropped to 194 lb., his level of consciousness brightened, and the muscular twitching decreased. The potassium level dropped to 4.7 mEq./l., but the BUN climbed to 150 mg. %. He was nauseated but did not vomit and there was no troublesome diarrhea.

Bacteriological studies showed a heavy growth of *Staphylococcus pyogenes* from the throat. A renal biopsy was performed on the 5th hospital day and cultures of the biopsy material were sterile. Antistreptolysin "O" titre was 168 units. Urine passed on the 6th hospital day contained 33 mEq./l. of sodium and 44 mEq./l. of potassium, and had an osmolarity of 352 m.osm./l. Repeated microscopic examinations of the urine showed the same features noted in the initial specimen.

During the last six days of his life the patient remained oliguric (urine output 0-200 c.c. per 24 hours). His general condition remained the same. With rigid fluid and electrolyte management his weight continued to decline by 1 to 2 lb. per day. On March 11 he developed watery diarrhea and became somnolent. Results of blood chemistry studies on that day showed a BUN value of 198 mg. %, bicarbonate of 21 mEq./l. and potassium of 4.4 mEq./l. A decision was made to dialyze the patient the next morning.

After periods of agitation and hypotension during the night of March 11, the patient gasped and died suddenly in the early hours of March 12, 1961.

CASE 2

A WHITE WOMAN, aged 63 years, developed shortness of breath on exertion and vague precordial pain in 1954, and swelling of the legs in 1956. In June 1956, she was found to have fluid in her right chest, for which a thoracentesis was performed. She had had a poor appetite and had lost a considerable amount of weight, strength and colour. The leg swelling was controlled fairly well by treatment at home. She had recently noted that she bruised easily after minor trauma.

FIRST ADMISSION

On October 8, 1956, she was admitted to the Royal Victoria Hospital complaining of nausea, vomiting, diarrhea, weakness, dizziness and burning on micturition of four days' duration. She gave a history of amputation of the left foot for injury at 12 years, perforative appendicitis at 16, herniotomy at 31 years, and four normal pregnancies, but otherwise no ill health till the onset of the present illness. Her father and mother had died at 56 and 65 years respectively, of coronary disease. Her husband died of coronary disease in 1950.

On examination she showed evidence of weight loss but was in no acute distress. Temperature was normal, heart rate 90 per minute and blood pressure 135/105 (subsequently 110/70). She weighed 123 lb. The fundi were considered normal for her age. The right lobe of the thyroid was noted to be enlarged, smooth and non-tender. There were dullness and diminished breath sounds at the right lung base, a soft apical systolic murmur, right costovertebral and right upper quadrant tenderness, a left midtarsal amputation and no other signs of note.

The urine specific gravity was 1.022. It was free of albumin and contained 20-30 red blood cells and 10-15 white blood cells per high-power field. Culture yielded a moderate growth of *Alcaligenes fæcalis*. Cystoscopy disclosed an inflamed bladder mucosa, clear urine from both ureters, normal pyelograms and questionable evidence of external pressure on the right ureter. The hemoglobin value was 96%, hematocrit 45%, and sedimentation rate 11 mm. in one hour. The total white cell count was 10,200, with slight neutrophilia. Clotting factors were normal. A chest roentgenogram and fluoroscopy showed densities in the lower parts of both pleural spaces consistent with moderate right and small left effusions or pleural thickening, obscuring the heart borders; the heart was difficult to define. Findings on barium enema examination were normal.

She was treated with digitalis, dimenhydrinate (Dramamine) (for nausea), sulfisoxazole and nitrofurantoin (Furadantin) successively for urinary tract infection. It was noted that she bled excessively from the bladder after cystoscopy and still showed microscopic hematuria at time of discharge on October 27, 1956.

SECOND ADMISSION

She was re-admitted on October 30, 1956, because of gross hematuria with clots observed the day after discharge, and vomiting of 24 hours' duration. She was flushed and looked chronically ill but had no fever. The physical signs were the same as on the previous admission, except that the eyes were noted to be somewhat prominent and staring; the blood pressure was 90/60; and the liver edge was palpable, smooth and slightly tender one fingerbreadth below the right costal margin. Pelvic examination and cervical cytology were negative. The urine specific gravity was 1.023 with 1 plus albumin, many red blood cells and a few white blood cells per high-power field and no casts. Hemoglobin value was 86%, hematocrit 41, and sedimentation rate 21. The white blood cell count was 5400. Platelet count and bleeding, clotting and prothrombin times were normal. The bone marrow showed some generalized hyperplasia, consistent with recent blood loss. She underwent cystoscopy

three times because of recurrent bleeding from the bladder. On one occasion two ulcerated areas on the posterior wall were coagulated. A biopsy showed inflammatory tissue. The third cystoscopy showed many areas of submucosal hemorrhage, interpreted as interstitial cystitis. Retrograde pyelograms were normal. Urine culture grew coliform bacteria and anaerobic streptococci. Treatment included administration of sulfonamides, nitrofurantoin (Furadantin), tetracycline and oleandomycin. Gross hematuria cleared within three weeks, but microscopic hematuria was again present at the time of discharge on December 2, 1956. Her blood pressure had averaged 120/70 and her weight had dropped from 121 lb. to 115 lb.

THIRD ADMISSION

She was re-admitted on March 2, 1957, for control of peripheral edema and shortness of breath which had returned gradually and had become refractory to digitalis, mercurials and acetazolamide (Diamox). She required two pillows at night and her weight had increased 30 lb. to 145 lb. She was dyspneic at rest. There were numerous ecchymoses scattered over her body and a right scleral hemorrhage was noted. Blood pressure was 140/90 and pulse rate 70, with numerous extrasystoles. The thyroid showed nodular enlargement of both lobes which were hard. Moist rales were heard in both lung bases, with dullness at the right base. Marked edema of the lower abdominal wall, sacrum and legs was present.

The urine showed a trace of albumin but was otherwise negative. Non-protein nitrogen value was 31 mg. %, total protein 5.32 g. %, albumin 4.15 g. %, globulin 1.17 g. %, cholesterol 200 mg. %, protein-bound iodine 6.5, I^{131} uptake 10.2% in 24 hours. Electrolyte determinations showed a low chloride value on admission, later rising to normal, and normal sodium and potassium values on three occasions.

FOURTH ADMISSION

She was re-admitted on September 29, 1957. She had seemed fairly well until July 1957 when edema of the legs reappeared and failed to respond to digitalis and diuretics and her weight rose 13 lb. When re-admitted she complained of edema of her legs, anorexia, drowsiness, nocturia (x 2), increased urgency, and easy bruising and bleeding. She was afebrile and looked thin, but had marked edema of the legs. Both lobes of the thyroid were grossly enlarged and firm. The blood pressure was 115/80 and pulse rate 96 and regular. Dullness and diminished breath sounds were present at the right base. The external jugular veins were distended, the right more than the left. The liver edge was palpable three fingerbreadths below the right costal margin. Ecchymotic areas were noted on the anterior chest wall and a brownish discolouration over the sacrum. The Rumpel-Leede test was positive.

The urine specific gravity was 1.010 with 2 plus albumin; there were a few more white blood cells than normal per high-power field, 0-24 red blood cells and tubular and granular casts. Urine culture grew *E. coli communior* and streptococcus species. The hemoglobin was 99%, hematocrit 51%, sedimentation rate 13 mm. in one hour, and white cell count 8800, with a normal differential count. The platelet count and bleeding, clotting and prothrombin times were normal. The electrophoretic pattern showed an elevation of alpha-2 globulin. The chloride level was 94 mEq./l., sodium 134 and potassium 6.2. A chest roentgenogram (October 2) showed cardiac enlargement, difficult to define, moderate pulmonary congestion and right pleural effusion. The electrocardiogram showed sinus rhythm, normal conduction, absent Q and notched R waves in V5 and 6 indicating left bundle branch block, and digitalis-type ST-T complexes in AVF, lead 3, V5 and V6. Treatment was continued with low salt diet, digitalis and occasional injections of mercurials. Improvement was transient and followed by progressive weight gain. The hemorrhagic manifestations persisted; there were ecchymotic areas and hematomata related to pressure and minor trauma but no petechial or small purpuric lesions. Gross hematuria was noted 10 days after admission, and cleared spontaneously in four days. Chlorothiazide was given without any effect on the edema. On November 8, prednisone therapy was commenced, with slight initial diuresis. On November 11 she vomited several times and complained of yellow streaks of light in her vision. That evening she developed severe epigastric pain and dyspnea and was observed to have a "poor colour". On November 12, dyspnea was greater and there were many rales at the lung bases. Her pulse rate was 84, with occasional extrasystoles, and blood pressure was 110/60. She became very anxious but slept well that night. On November 13, at 6.30 a.m. she called for a bedpan and a few minutes later was found dead in bed.

PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

The midwife may be defined as a person attempting to practise obstetrics without complete or even adequate medical education. The tolerance of such persons is an anomaly in an enlightened civilization. The midwife is a relic of mediævalism, unhappily extant in the countries of the Old World, but whose persistence in our own community should not be encouraged by any form of recognition.—*The Boston Medical and Surgical Journal;* quoted in the *Canadian Medical Association Journal,* 1: 343, April 1911.

Canad. M. A. J.
May 13, 1961, vol. 84

INFORMATION FOR CANADIAN DOCTORS ON

FINANCIAL ASSISTANCE AVAILABLE FOR GRADUATE OR POSTGRADUATE MEDICAL STUDY

in

CANADA - UNITED STATES - EUROPE

(PART 2*)

Through its Journal, The Canadian Medical Association is pleased to provide up-to-date information on financial assistance that is available to facilitate the graduate and/or postgraduate medical education of Canadian doctors. Owing to space limitations, we are not in a position to publish the complete list of medical award classification at this time. Please refer to subsequent issues of the Journal, if the subject in which you are interested is not listed herein.

Unless otherwise indicated, the value of the awards will be quoted in the currency of the country mentioned. As entry regulations into a foreign country vary, it is recommended that the applicant for postgraduate study first investigate all details through the Embassies of the foreign countries concerned. Applicants should satisfy themselves whether medical registration in the jurisdiction of the award is or is not a requirement to hold the postgraduate post in the country selected.

In so far as entry into the United States is concerned, simply communicate with the U.S. consular office nearest your place of residence. These offices are located in the following cities: St. John's, Newfoundland; Halifax, Nova Scotia; Saint John, New Brunswick; Quebec, Quebec; Montreal, Quebec; Ottawa, Ontario; Toronto, Ontario; Windsor, Ontario; Winnipeg, Manitoba; Calgary, Alberta; Edmonton, Alberta; and Vancouver, British Columbia.

It is understood that a Canadian citizen entering the United Kingdom must have a valid passport but that no visa is necessary. Application forms for passports can be obtained at any large Canadian Post Office and should be completed and sent to the Chief Passport Officer, Ottawa, Ontario.

Name of Award	Field of Study	Where Tenable	Value	Number Available	Duration	Conditions	Apply to
INTERNAL MEDICINE — CANADA							
The Canadian Arthritis and Rheumatism Society Postgraduate Clinical Training Fellowships	Internal medicine, with special emphasis on rheumatology	Any centre in or beyond Canada approved by the Society's Committee on Research and Professional Education and The Royal College of Physicians and Surgeons of Canada	$2600—$5000 per annum depending upon candidate's training, experience and domestic responsibilities	Unspecified	One year (renewable on application)	Committee must be satisfied that candidate has reasonable expectation of obtaining Certification in Medicine or Fellowship of Royal College of Physicians (Can.) following completion of one or two years on fellowship	The Canadian Arthritis and Rheumatism Society, 900 Yonge Street Toronto 5, Ont., by October 22
The Canadian Arthritis and Rheumatism Society Medical Research Fellowships	Any basic medical science, where the objectives of the Fellowship are deemed significant to the rheumatic diseases	Canada	$2600—$5000	Not specified	One year (renewable on application)	Candidate must be either a graduate of a recognized medical school, or hold a master's degree or a doctorate of philosophy or science in a suitable field from a recognized university	The Canadian Arthritis and Rheumatism Society 900 Yonge Street Toronto 5, Ont.
American College of Physicians: Elizabeth Archbold Bowes Travelling Scholarship	Internal medicine	Canada or United States	$400 for travel expenses.	One	One month, more or less	Candidate must be an associate of the College and a Canadian citizen. To provide an opportunity for worthy young physicians to spend a month, more or less, as visiting Fellows at some institution(s) for observation and postgraduate study	The American College of Physicians, 4200 Pine Street, Philadelphia 4, Pa.
American College of Physicians: A. Blaine Brower Travelling Scholarship	Internal medicine and allied fields	Canada or United States	$400 for trave expenses	Two	One month, more or less	Candidate must be an Associate of the College; Canadians eligible. To provide an opportunity for worthy young physicians to spend a month, more or less, as visiting Fellows at some institution(s) for observation and postgraduate study	The American College of Physicians, 4200 Pine Street Philadelphia 4, Pa.
American College of Physicians: Mead Johnson Postgraduate Scholarship	Internal medicine	Canada or United States	$1000 per annum	Ten	One year	Recipients shall be individuals who intend to practise internal medicine; who appear to possess attributes for	The American College of Physicians, 4200 Pine Street Philadelphia 4, Pa., by October 1 for scholarships to begin the following July 1

*See also page 1038, issue of May 6.

Name of Award	Field of Study	Where Tenable	Value	Number Available	Duration	Conditions	Apply to
INTERNAL MEDICINE — CANADA							
						success in that specialty. Awards open to interns or residents with some preference to residents	
American College of Physicians Research Fellowships	Internal medicine and/or pediatrics	United States or Canada	$6500 first year, $7500 second year, $8500 third year	Two	A term of three years	Open to qualified graduates to provide an opportunity for research in any science basic to medicine or in medical education, or both. Candidates must be proposed by the Chairman of the Department of Medicine in any institution in the United States or Canada with a recognized program of medical education and research. Recipients shall devote a minimum of 80% of time to research, regardless of type of appointment held in any given institution	The American College of Physicians, 4200 Pine Street, Philadelphia 4, Pa., not later than October 1
American College of Physicians: Alfred Stengel Travelling Fellowship	Internal medicine	United States or Canada	$500 for travel expenses	One	One month, more or less	To provide an opportunity to a resident of advanced standing in Medicine, who during his third or fourth year desires to travel to some medical centre for a short period of study and observation	The American College of Physicians, 4200 Pine Street, Philadelphia 4, Pa., not later than October 1
University of Toronto: Frances Esther Hutchison Fellowship	Internal medicine	University of Toronto	Income from $50,000	One	One year	Open to graduates in medicine of any approved university for post-graduate study and for promotion of research. Award made on recommendation of Head, Department of Medicine	Professor of Medicine, University of Toronto, Toronto 5, Ont.
University of Toronto: Archibald Hutchison Fellowship	Internal medicine	University of Toronto	Income from $50,000	One	One year	Open to graduates in medicine of any approved university for post-graduate study and for promotion of research. Award made on recommendation of Head, Department of Medicine	Professor of Medicine, University of Toronto, Toronto 5, Ont.
University of Toronto: Alexander McPhedran Research Fellowship in Clinical Medicine	Clinical medicine	University of Toronto	Unspecified	One	One year	Graduate in medicine, for investigation in clinical medicine	Professor of Medicine, University of Toronto, Toronto 5, Ont.
University of Toronto: Anna Bradbury Springer Award	Study of chronic nonmalignant diseases of gastro-intestinal tract	University of Toronto	Unspecified	One or more	One year	Graduate in medicine enrolled in the Division of Postgraduate Medical Education, University of Toronto	Director, Division of Postgraduate Medical Education, University of Toronto, Toronto 5, Ont.
INTERNAL MEDICINE — UNITED STATES							
Western Reserve University (School of Medicine): (a) Charles F. Hoover Memorial Fellowship (b) Dr. Marie Zakrschefska Fellowship (c) Flora G. Kaufholz Fellowship	Internal medicine	Western Reserve University	(a) $995 per annum; (b) $525 per annum; (c) $975 per annum	One each of (a), (b) and (c)	One year (renewable)	Open to qualified graduates	The Dean, School of Medicine, Western Reserve University, 2065 Adelbert Road, Cleveland 6, Ohio
American College of Physicians Research Fellowships	Internal medicine and/or pediatrics	United States or Canada	$6500 first year, $7500 second year, $8500 third year	Two	A term of three years	Open to qualified graduates to provide an opportunity for research in any science basic to medicine or in medical education, or both. Candidates must be proposed by the Chairman of the Department of Medicine in any institution in the United States or Canada with a recognized program of medical education and research. Recipients	The American College of Physicians 4200 Pine Street Philadelphia 4, Pa. not later than October 1

Name of Award	Field of Study	Where Tenable	Value	Number Available	Duration	Conditions	Apply to
INTERNAL MEDICINE — UNITED STATES							
						shall devote a minimum of 80% of time to research, regardless of type of appointment held in any given institution	
American College of Physicians: Alfred Stengel Travelling Fellowship	Internal medicine	United States or Canada	$500 for travel expenses	One	One month, more or less	To provide an opportunity to a resident of advanced standing in medicine, who during his third or fourth year desires to travel to some medical centre for a short period of study and observation	The American College of Physicians, 4200 Pine Street, Philadelphia 4, Pa., not later than October 1
American College of Physicians: Elizabeth Archbold Bowes Travelling Scholarship	Internal medicine	Canada or United States	$400 for expenses	One	One month, more or less	Candidate must be an Associate of the College and a Canadian citizen. To provide an opportunity for worthy young physicians to spend a month, more or less, as visiting Fellows at some institution(s) for observation and postgraduate study	The American College of Physicians, 4200 Pine Street, Philadelphia 4, Pa.
American College of Physicians: The A. Blaine Brower Travelling Scholarships	Internal medicine and allied fields	Canada or United States	$400 for travel expenses	Two	One month, more or less	Candidate must be an Associate of the College: Canadians eligible. To provide an opportunity for worthy young physicians to spend a month, more or less, as visiting Fellows at some institution(s) for observation and postgraduate study	The American College of Physicians, 4200 Pine Street, Philadelphia 4, Pa.
American College of Physicians: Mead Johnson Postgraduate Scholarships	Internal medicine	Canada or United States	$1000 per annum	Ten	One year	Recipients shall be individuals who intend to practise internal medicine; who appear to possess attributes for success in that specialty. Awards open to interns or residents with some preference to residents	The American College of Physicians, 4200 Pine Street, Philadelphia 4, Pa., by October 1 for scholarships to begin the following July 1
MEDICAL RESEARCH — UNITED KINGDOM							
Beit Memorial Fellowships for Medical Research: (a) Junior Fellowships (b) Fourth Year Fellowships (c) Senior Fellowships	Medical research	United Kingdom	(a) £900 per annum with £50 increments for second and third year; (b) £1100 per annum; (c) £1300 per annum	Unspecified	(a) Three years (b) One year (c) Three years	The Fellowships are open to any person without restriction of nationality, who at the date of election has taken a degree in any faculty in any university in H.M. Dominions, Protectorates and Mandated Territories, India, Pakistan and the Republic of Ireland approved by the Trustees, or a medical diploma registrable in the U.K.	Sir Roy Cameron, F.R.S., Secretary, Beit Memorial Fellowships, University College Hospital Medical School, University Street, London, W.C. 1, England, by April 1
Beit Memorial Fellowships	Medical research	United Kingdom	£900 to £1000	Unspecified	Three years	Available to graduates of any university of the British Empire who hold a medical degree or diploma registrable in the United Kingdom. Senior fellowships given to former holders of Junior fellowships	Sir Roy Cameron, F.R.S., Secretary, Beit Memorial Fellowships for Medical Research, U.C.H. Medical School, London, W.C. 1, England or The Canadian Medical Association, 150 St. George St., Toronto 5, Ont., before April 1
MEDICAL RESEARCH — UNRESTRICTED							
Squibb Institute for Medical Research Fellowships and Grants	Medical research	Unrestricted	Variable	Not limited	One year (renewable)	Candidates should present as much information as possible on the subject of investigation, the institution where it will be pursued and on support of	Chairman, Committee on Fellowships and Grants, Squibb Institute for Medical Research (Division of Olin Mathieson Chemical Corporation), 745 Fifth Ave., New York 22, N.Y.

Name of Award	Field of Study	Where Tenable	Value	Number Available	Duration	Conditions	Apply to
MEDICAL RESEARCH — UNRESTRICTED							
						the project. Applications are considered individually on the basis of facts involved in the person of the applicant, or the nature of the proposed study	
MEDICAL SCIENCES — CANADA							
McGill University: Sir Edward W. Beatty Memorial Scholarships	Research or special training in a clinical specialty	McGill University; if scholar is a graduate in medicine of McGill, work may be undertaken at McGill or elsewhere	Not less than $1500	Two	One year	Open to postgraduate students in Faculty of Medicine registered in a course of study leading to a diploma in a clinical specialty. Holder is expected to devote scholarship year to research or some form of special training	Secretary, Faculty of Medicine, by February 1
Fellowships in Medical Specialties	Cardiology, hematology, gastroenterology, neurology, rheumatic diseases, diseases of metabolism	Queen's University	Stipend according to experience of graduate	Two	One year	Unspecified	Professor of Medicine, Queen's University, Kingston, Ont.
J. B. Collip Fellowships	Medical research in anatomy, bacteriology, biochemistry, histology, pathology, pharmacology and physiology	McGill University	$1500 to $3000	Three of these Fellowships in all	One academic year	Candidate must have M.Sc. or Ph.D. degree in subject of study, or have degree in medicine	Secretary, Faculty of Medicine, McGill University, Montreal, P.Q., by February 1
National Health Grant bursaries for postgraduate training (special grants from the Department of National Health and Welfare to the Provincial Governments)	Bursary assistance considered for postgraduate training necessary for new or expanded health services in province-wide programs for health	Canadian centres preferred; United States and other countries considered if necessary to training	Max. $250 plus travel, tuition and book allowance	Unspecified	One to three years	Applicant required to enter into a contract with province to provide a reasonable return-in-service in the appropriate health field within the province	Deputy Minister, Department of Health of the province where the applicant is prepared to provide a suitable return-in-service
University of Toronto: George Brown Memorial Scholarship	Original research in medical science	Any approved university or hospital	$1500	One every three years	One year	Open to a Doctor of Medicine of University of Toronto of not more than 3 years' standing who has taken a high place in the professional examinations of the four medical years and in Biology of the second premedical year. Holder required to devote his time to original research, either laboratory or clinical	The Dean, Faculty of Medicine, University of Toronto, Toronto 5, Ont., not later than March 1
Dalhousie University: Ross Stewart Smith Memorial Fellowship	Research in clinical medicine or in basic medical science	Dalhousie University	$2500	One	One year	Awarded to a student on graduation at the end of the rotating internship and may be held by him during any one year of his later postgraduate program. That year must be spent in medical research	The Dean, Faculty of Medicine, Dalhousie University, Halifax, N.S.
MEDICAL SCIENCES — CANADA (Normally)							
Medical Research Council Medical Research Fellowships	Medical sciences	Normally at Canadian universities; under special circumstances at an institution outside Canada	(a) $3000 per annum; (b) $3200 per annum; (c) $3200 to $5000 per annum (plus travel expenses)	Limited	One year (renewable)	Candidates must be graduates of approved medical schools or hold the Ph.D. degree in a medical science. Open to men and women. Applicants for a first award must not be more than 35 years of age on March 1 of the year of application. (a) open to candidates with M.D. degree who have had no internship after graduation. (b) open to graduates in medicine with one year's internship. (c) open to more experienced candidates, the amount of the award depending on candidate's training and achievement in research	The Secretary, Medical Research Council, National Research Building, 100 Sussex Drive, Ottawa 2, Ont.

Name of Award	Field of Study	Where Tenable	Value	Number Available	Duration	Conditions	Apply to
MEDICAL SCIENCES — CANADA							
The John Alexander Stewart Fellowship	Research in medicine	Queen's University	$2400	Two	One year	Available annually commencing 1962	Professor of Medicine, Queen's University, Kingston, Ont.
Henry Charles Fowler Fellowship	Preventive medicine	Queen's University	Approx. $1200	One	One year	Unspecified	Professor of Preventive Medicine, Queen's University, Kingston, Ont.
William Spankie Memorial Endowment Fund	Medical research	Queen's University	$1480	One	One year	Unspecified	Principal, Queen's University, Kingston, Ont.
John and Mary Markle Foundation Grants for Scholars in Medical Sciences	Medical science and/or teaching	Canadian schools of medicine	$30,000 payable at the rate of $6000 per annum	Variable, not exceeding twenty-five	Five years	Candidate must be graduate, holding such degrees as are acceptable for faculty rank by nominating university. Must have a major interest in medical research and/or medical teaching	Applicants are nominated by the Deans of Medical Schools, prior to December 1. Nominations are to be sent to The John and Mary Markle Foundation, 511 Fifth Avenue, New York 17, N.Y.
Canadian Life Insurance Officers Association: Medical Research Fellowships	Medical research	Canadian schools of medicine	$5000 including laboratory and other expenses	One for each Canadian medical school	One year (renewable for a further two)	Candidate should have particularly strong interest in research or teaching; must have recommendation from Dean of Medical School	The Secretary, Standing Committee on Public Health, The Canadian Life Insurance Officers Association, 302 Bay Street, Toronto, Ont., by February 14
Province of Nova Scotia Postgraduate Bursaries	Physical medicine, hospital administration, pathology, psychiatry, neurology, tuberculosis, public health, child and maternal health	Nova Scotia; under special circumstances, elsewhere in Canada or in the U.S.A.	$200 per month; $250 for candidates with dependants; tuition and $35 book allowance	Limited	One year (renewable for second; occasionally for third)	Trainee must return to or accept a full-time salaried position in health or hospital services of Nova Scotia. For initial year of the bursary trainee has a two-year commitment and an additional year commitment for each additional year of training	Deputy Minister, Department of Public Health, Halifax, N.S.
Province of Ontario Postgraduate Bursaries	Public health, industrial health, psychiatry	Ontario universities; in special circumstances an institution elsewhere in Canada or the U.S.A.	$200 per month, plus $50 for dependents; University fees are also paid	Unspecified	Unspecified	Bursary assistance conditional upon a signed agreement to return service, in a public salaried capacity in the Province of Ontario for one year for each academic year of training, or part thereof. Candidates acceptable to Province must also be acceptable to the training institution and the Federal authorities	Department of Health, Province of Ontario, Toronto, Ont.
R. Samuel McLaughlin Foundation: Travelling Fellowships	Medical science	Unrestricted	$250 per month, extra allowance for travel expenses	Unspecified	Up to twelve months	Candidates may be men or women 25 to 35 years of age; must be nominated by dean of medical school and head of clinical department; must have been selected for appointment on the permanent clinical staff of some Canadian medical school and one of its affiliated hospitals; shall have completed undergraduate and internship training and have shown special aptitude for teaching or research	The R. Samuel McLaughlin Foundation, Dr. J. A. MacFarlane, Faculty of Medicine, University of Toronto, Toronto 5, Ont.
MEDICAL SCIENCES — CANADA							
Graduate Teaching Assistantships	Basic sciences	University of Alberta Faculty of Medicine	$2400	Indefinite	One year	Available to graduate students	Faculty of Graduate Studies, University of Alberta, Edmonton, Alta.
MEDICAL SCIENCES — FRANCE							
Scholarship of the French Government: Laval University and University of Montreal		Recognized hospital in France	Room and board plus $150 per month	Approx. twenty per annum	One year	Candidate must be graduate of either Laval University or Montreal University and be recommended by the Dean of Faculty of Medicine of either university	Embassy of France, Ottawa, Ont.
Scholarship of the Government of France: Laval University		France	$1000 per annum	Usually one each year	One year	Candidate must be recommended by university authorities	Embassy of France, Ottawa, Ont.

(To be continued)

OBITUARIES

DR. JAMES E. BLOOMER, 78, of Moose Jaw, Sask., died there on April 7. Dr. Bloomer had practised in Moose Jaw for more than half a century after graduating from the University of Manitoba Medical School in 1909. During World War I he served overseas as medical officer and, after demobilization, returned to his Moose Jaw practice. He had been active in cancer research for several years.

Surviving Dr. Bloomer are his widow, son and daughter.

DR. WILLIAM J. CORRIGAN, 89, died April 8 in Toronto General Hospital, with which he had been associated for more than fifty years. Born and educated in Milton, Halton County, Dr. Corrigan taught school for two years before attending Trinity Medical School, and graduated with the first Trinity class after its amalgamation with the University of Toronto in 1905. Dr. Corrigan first practised in Minnesota for two years before returning to Toronto to open his own outpatient clinic. He was an honorary life member of the Academy of Medicine.

He is survived by his widow and daughter.

DR. JOHN H. GEDDES, 62, assistant professor of medicine at the University of Western Ontario, died at his home in London, Ont., on April 16. Dr. Geddes studied internal medicine in the United States after graduating from the University of Western Ontario Medical School in 1924. Later he was appointed to the staff of Victoria, Westminster and St. Joseph's hospitals.

During World War I he enlisted with the Canadian Air Force, and in World War II served overseas as lieutenant-colonel in the Royal Canadian Army Medical Corps.

An active member of several provincial medical committees, he was a past president of the London Academy of Medicine and had served as a director of the Ontario Medical Association.

He is survived by his widow and daughter.

DR. EARL M. JONES, 63, died at St. Joseph's Hospital, Hamilton, on March 11. A graduate of the University of Toronto Medical School in 1923, Dr. Jones served his internship at the Hamilton General Hospital, practised for three years in Millbank, Ontario, and opened a practice in Jarvis where he served the local community for many years.

He is survived by his widow and daughter.

DR. JULES LAFLEUR, 52, died while undergoing surgery at the Hôtel-Dieu de Montreal, on March 6. Former mayor of Lachute from 1953 to 1955 and district coroner for many years, Dr. Lafleur was born and educated in Lachute and received his B.A. from the Collège Ste-Marie, Montreal. He graduated from the University of Montreal Medical School in 1937 and practised in his home town from 1938.

He is survived by his widow and ten children, six sons and four daughters. One son, Richard, is a first-year medical student at the University of Ottawa.

DR. JAMES J. McCANN, 74, former Revenue Minister in both the Mackenzie King and St. Laurent Liberal governments, died suddenly in Ottawa on April 11.

Born at Perth, Ontario, he graduated from Queen's University Medical School as a gold medallist in 1909, served as medical officer with the Canadian Pacific Railway for two years, and in 1911 took a postgraduate course at the University of Chicago. One year later he opened a practice in Hamilton, where he played two seasons with the Hamilton Tigers.

In 1913 Dr. McCann moved to Renfrew where he continued the practice of his late brother-in-law, Dr. B. C. Connelly, and became coroner for Renfrew County, serving in this capacity for thirty years. He was also Medical Officer of Health of the town of Renfrew for many years.

He had been president of the Ontario Health Officers Association and the Canadian Public Health Association.

Dr. McCann is survived by his widow.

DR. JAMES J. McCANN

An Appreciation

The death of Dr. J. J. McCann at the age of 74 on April 11, 1961, removes a colourful figure who achieved prominence in his profession as well as in politics and government. Jim McCann was a stalwart in physique and in his approach to the problems which confront those who assay the heights of public office. At Queen's, where he graduated with high distinction in 1909, he was a football player and, as a rugged lineman, he appeared to revel in the rough going. He appeared also to revel in the practical politics of the Ottawa Valley which has little consideration for the timid. He represented the constituency of Renfrew South as Liberal member from his election in 1935 until his enforced retirement in the 1957 election, and in the interval held the Cabinet posts of Minister of National War Services and Minister of National Revenue. James McCann was a general practitioner of the good old school and, in addition, he was a district coroner and Medical Officer of Health of the town of Renfrew for many years. Before and after his election to Parliament he was a familiar and respected figure at meetings of the Ontario Health Officers Association and in 1939 he was President of the Canadian Public Health Association. Here is the example of the small town doctor who served his country in high places, and although the portfolios which he held appeared to be far removed from medicine he discharged the duties ably and unassumingly and exerted considerable influence on the health programs of the Federal Government over many years. We, who are frequently exhorted to have doctors take a more active role in government, can look to the career of James McCann as the model of the good doctor who served well in local and national affairs.

A.D.K.

DR. THOMAS W. MacLEAN, 64, Medical Officer of Health for Plympton Township, died at the Sarnia (Ont.) General Hospital on March 28. Born in Springville, N.S., Dr. MacLean served overseas with the Canadian Expeditionary Force during World War I.

He entered Dalhousie University Medical School after demobilization and graduated in 1924. After graduation Dr. MacLean practised in Scotsburn and Westvillen, Nova Scotian mining towns, where he endeared himself to his country patients for many years. Seven years ago he went to Sarnia to join the St. Clair Medical Centre. As medical officer for Twilight Haven, Petrolia, he became especially attached to the Haven's aged and infirm patients. He had been a director of the Children's Aid Society.

He is survived by his widow, two sons and three daughters.

DR. WILLIAM A. MACLEOD, 78, former member of the Nova Scotia Provincial Legislature, died in Aberdeen Hospital, New Glasgow, on April 12. Known throughout Pictou County as "Our country doctor", he had attended the families of Hopewell citizens for almost half a century, travelling around his country practice by horse and wagon until presented with a car by grateful patients.

As a Conservative member of the Provincial Legislature from 1956 until his retirement in 1960, Dr. Macleod fought to improve rural paving facilities throughout Pictou County. Born in Gairlock, N.S., he graduated from Dalhousie University Medical School in 1908 and first opened an office in River Hebert, where he practised for four years before going to Hopewell.

Dr. Macleod is survived by his widow and son.

DR. FREDERICK C. MYERS, 63, died in the Welland County General Hospital on March 25. Born and educated in St. Mary's, Ont., Dr. Myers graduated from Toronto University Medical School in 1922 and practised in the Fonthill district for many years.

He is survived by his widow and daughter.

DR. ROBERT L. NESBITT, 49, died in Ottawa on April 6. Dr. Nesbitt had practised in Ottawa for 20 years after his graduation from Queen's University in 1937.

He is survived by his widow and two sons.

DR. THOMAS M. SAVAGE, 64, died at his home in Guelph, Ont., on April 12. Son of the late Dr. W. F. Savage, he was born in Elora and graduated from the University of Toronto Medical School in 1913. Following service as a medical officer with the French and Canadian armies during World War I, Dr. Savage opened a practice in Guelph and continued to practise there until his death.

He is survived by his widow, two sons and a daughter.

HAMILTON BAILEY

AN APPRECIATION

To students of surgery, undergraduate and postgraduate, in the British Commonwealth and in many other parts of the world, the name Hamilton Bailey is a memorable one. I believe that it was by his writing —more than that of anyone else—that British surgery became esteemed and renowned throughout the world. In the period between the wars—to my generation of medical students—Bailey's "Demonstrations of Physical Signs in Clinical Diagnosis", Bailey & Love's "Textbook of Surgery" and Bailey's "Emergency Surgery" were perhaps the best known examples of British surgical writing. They were lucid, they were well illustrated and with rare judgment they pointed up what was important in the welter of information a student has to assimilate. The repeated editions of these works is ample evidence of the sustained demand by succeeding generations of students.

It has seemed to some of us from the "Dominions" rather curious that in his own country there appeared to be less than full recognition of Hamilton Bailey's importance in the growth of the reputation of British surgery throughout the world. Without entering into the subtleties of the origin of honours lists, it has seemed surprising that a name, towering across the borders, should not have parallel recognition within. But such are the ways of contemporary men.

Hamilton Bailey had among his many gifts great charm and friendliness. Not only his clinics but his home was always open to visiting students without regard to race, colour or creed. Innumerable "colonials" found a warmth and hospitality so hard for the shy, unheralded visitor to find. Veta and Hamilton Bailey's home became a haven for so many of us on subsequent visits to England. There friendships were formed enduring beyond time and space.

Thus in many parts of the world there is a real personal sense of loss in the death of a great man and a close friend. Only Veta can understand this fully and her we face from many corners of the world in warm and deep sympathy.

ALAN KLASS, B.A., M.D., F.R.C.S.(Edin.),
F.R.C.S.[C], F.I.C.S.

PUBLIC HEALTH

SURVEILLANCE REPORTS OF EPIDEMIC OR UNUSUAL COMMUNICABLE DISEASES

INFLUENZA

The Dominion Bureau of Statistics reports that the deaths due to respiratory infection remain within the expected normal limits for the season. Absenteeism due to illness, as reported by the Labour Force Survey, is also within normal seasonal limits.

The Surgeon General of the Canadian Forces Medical Service will discontinue the telegraphic reporting of influenza-like disease on April 1, 1961. The reports received from the Navy, Army and Air Force Commands did not indicate any occurrence of influenza outbreaks.

Approximately 70 cases of influenza-like disease have been reported from Carol Lake (Labrador). Symptoms consist of pyrexia up to 104° F., headaches, rigors, and joint and back pains. Seventeen cases have been hospitalized with pneumonia and hemoptysis. The population totals about 1500.

Outbreaks of influenza-like disease have been reported from Mount Carmel and St. Catherine's, Newfoundland. The main complaints are severe bronchitis, headaches, chills, fever, back and limb pains. Both sexes and all ages are equally affected.

Influenza virus A2 has been isolated in Ottawa, Ont., from five cases. All of the patients are service personnel. Three of them were hospitalized at the Canadian Forces Hospital, Rockcliffe, and the other two were seen at the M.I.R. Two of the hospitalized patients are United States Air Force officers and the other three patients are Canadian Army servicemen.

SUMMARY OF REPORTED CASES OF NOTIFIABLE DISEASES IN CANADA*
ISSUED BY THE PUBLIC HEALTH SECTION, DOMINION BUREAU OF STATISTICS

Disease	Week ended (1961): March 4	March 11	March 18	March 25	Cumulative total since beginning of year: 1961	1960
Brucellosis (Undulant fever) (044)	2	—	—	3	19	12
Diarrhea of the newborn, epidemic (764)	4	4	2	—	16	13
Diphtheria (055)	1	5	—	—	30	9
Dysentery (045, 046, 048)	51	27	48	31	466	858
(a) Amebic (046)	—	—	—	—	5	1
(b) Bacillary (045)	26	12	19	7	228	757
(c) Other and unspecified (048)	25	15	29	24	233	100
Encephalitis, infectious (082.0)	—	—	—	—	—	—
Food poisoning: (049.0, 042.1, 049.2)	20	13	31	18	270	371
(a) Staphylococcus intoxication (049.0)	—	—	10	3	13	236
(b) Salmonella with food as vehicle of infection. (042.1)	19	13	21	15	255	127
(c) Unspecified (049.2)	1	—	—	—	2	8
Hepatitis, infectious (including serum hepatitis) (092, N998.5)	264	234	224	194	2,799	1,785
Meningitis, viral or aseptic (080.2, 082.1)	—	4	7	2	36	58
(a) Due to Poliovirus	—	1	—	—	2	23
(b) Due to Coxsackie virus	—	—	2	—	3	1
(c) Due to ECHO virus	—	—	—	—	—	1
(d) Other and unspecified	—	3	5	2	31	33
Meningococcal infections (057)	3	6	1	4	37	50
Pemphigus neonatorum (Impetigo of the newborn) (766)	—	—	—	—	—	4
Pertussis (Whooping cough) (056)	76	63	72	48	914	1,502
Poliomyelitis, paralytic (080.0, 080.1)	—	—	2	2	14	64
Scarlet fever and Streptococcal sore throat (050, 051)	462	533	314	333	4,765	9,773
Typhoid and Paratyphoid fever (040, 041)	5	5	1	10	56	91
Venereal disease: (020-039)	370	320	366	383	4,270	3,873
(a) Gonorrhea (030-035)	322	270	320	335	3,736	3,408
(b) Syphilis (020-029)	48	50	46	48	533	462
(c) Other† (036-039)	—	—	—	—	1	3

*Figures for the Yukon are received four-weekly and are, therefore, shown in the cumulative totals only.
†Including chancroid, granuloma inguinale and lymphogranuloma venereum.

Further information has been received on the influenza cases among service personnel in Ottawa. The majority of cases occurred among United States Air Force personnel stationed in Ottawa. The first case on February 6, 1961, was a sergeant who had just arrived from Stewart Air Force Base, New York. During the following week about 60 cases occurred among service and civilian personnel working in the United States Air Force offices. Most of the United States service personnel affected were vaccinated against influenza last November.

According to the local medical representative of the United States Air Force, no cases of influenza have been reported from Stewart Air Force Base, but the sergeant in question did stop in transit for one day at Idlewild Airport, where he may have contracted the infection.

TULAREMIA

A case of tularemia has been reported from Brampton, Ont.

ANTHRAX

A case of anthrax has been reported from Oxford-on-Rideau, Ont.

TRICHINOSIS

Six cases of trichinosis have been reported in the Province of Quebec for the week ending March 4, 1961—three from Jonquière and three from Jacques-Cartier, Rouville County, and Montreal North.

TETANUS

A case of tetanus, in a male aged 18 years, has been reported from Lethbridge, Alta.

MENINGOCOCCAL MENINGITIS

Two cases of meningococcal meningitis have been reported from Prince Albert, Sask. The first, in a 10-month-old baby, occurred on February 10, 1961, and the second, in a 3-month-old baby, on March 3. There is no known connection between these cases.

International Reports

INFLUENZA

United Kingdom

Influenza has continued to decline in all parts of England and Wales. The number of influenza deaths has continued to decrease. For the week ending March 18, 1961, 104 influenza deaths were reported, compared with 197 the week before.

SMALLPOX

Spain

On March 21, 1961, the public health authorities announced that the smallpox outbreak in Madrid could now be considered as completely cleared. Since February 6, when the first case was diagnosed, a total of 16 cases and 3 deaths were reported. The chronology of the outbreak was as follows.

The primary case arrived from Bombay on January 27 and was diagnosed on February 6. The secondary case occurred on February 21; 13 further cases between February 26 and March 4; and 1 case in the week March 5-11. The first death (the primary case) occurred on February 14 and the other two deaths on March 12.

Epidemiology Division, Department of
National Health and Welfare.
Ottawa, March 25, 1961.

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May 13, 1961, vol. 84

BOOK REVIEWS

SURGICAL DISEASES OF THE CHEST. Edited by Brian Blades. 580 pp. Illust. The C. V. Mosby Company, St. Louis, Mo., 1961. $22.00.

This book, to which 18 authors have contributed, is edited by Dr. Brian Blades, Professor of Surgery, The George Washington University School of Medicine, Washington, D.C., and quite fittingly dedicated to the late Professor Evarts Ambrose Graham, who played such an important role in the development of the surgery of the chest and in the training of so many who today are important figures in this field of surgery. The editor states in the preface that the book was written not only for surgeons but also for medical students and medical practitioners. Obviously it could not have been easy to write a book which would meet the requirements of these groups whose needs differ so widely, but on the whole the authors have been successful. Undoubtedly the surgical specialist will at times wish for more detail and the medical student for less, but each will find the essentials. Quite fittingly, the first chapter is devoted to a brief presentation of the basic physiology which anyone attempting to do thoracic surgery should know.

In the chapter on chest trauma one is left with the impression that in the presence of a pneumothorax associated with a major air leak it is sufficient to establish water-seal trap drainage. The importance of using an adequate controllable suction pump such as an Emerson might well have been emphasized. The important part that a properly equipped respiratory unit may play in severe chest trauma could well have been mentioned.

One is rather surprised to learn that "Empyema is a synonym for abscess and empyema thoracis is, therefore, an abscess of the pleura, which implies a localized collection of pus in the pleural cavity." This is, of course, not strictly accurate. Dorland defines empyema as an "accumulation of pus in a cavity of the body especially in the chest". The whole pleural space may be involved without any localization whatever and it is still empyema. Pus may be thick or thin and still be pus. It is apparent that the author wishes to stress the importance of avoiding open drainage until the empyema has been reduced to a localized collection of pus. One would have liked to see more emphasis placed upon the importance of adequate treatment by aspiration and the instillation of the appropriate antibiotic from the moment pus cells and bacteria are found in the pleural space, because if this is done the need for surgical drainage will arise only rarely.

One is also surprised at the statement that the most common cause of lung abscess is the aspiration of infected material during or after operations. This may have been true 30 years ago but surely with modern anesthesia a relatively small percentage of lung abscesses arise in this way.

These are examples of minor shortcomings which no doubt will be corrected in a future edition. They do not detract seriously from the usefulness of the book, which will be a worthwhile addition to the library of those with a special interest in thoracic surgery or the far larger group who find themselves forced to deal occasionally with chest problems.

CUTANEOUS MANIFESTATIONS OF THE RETICULOENDOTHELIAL GRANULOMAS. Edited by Samuel M. Bluefarb. 442 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1960. $16.00.

This monograph will serve as a reliable reference work for those practising internal medicine, pediatrics and dermatology.

The volume is divided into four separate sections, including lipidoses, systemic reticuloendothelial granulomas, sarcoidosis, and mastocytosis. In each instance, prominent authorities review their subject from the historical, theoretical, clinical and pathological viewpoints. Coverage is exhaustive, and bibliographies are extensive.

Tuberculosis, leprosy and syphilis have been properly excluded, and this has enhanced the value of the monograph.

One feels that the lipidoses have been forced into this monograph, and might better be discussed in a separate volume. The actual coverage is excellent, however, and a preliminary description of the chemistry and physiology of lipids helps in understanding this complex group of diseases.

Sarcoidosis is reviewed in an impartial manner, no easy feat with such a controversial "disease". The authors carefully refrain from positive opinions concerning the relationship of sarcoidosis and tuberculosis. They also do not emphasize the sharp differences between sarcoidosis in the Negro and the white. A large part of the review is devoted to clinical and laboratory findings, which provides a good source of such information for the clinician.

The section on systemic reticuloendothelial granulomas is mainly concerned with the triad of closely related diseases — Letterer-Siwe disease, Schüller-Christian disease, and eosinophilic granuloma. These conditions are quite logically discussed as variants of a single basic disease process, and the gradual development of this concept over the past 67 years makes fascinating reading. The extensive review of cutaneous and other clinical findings will be of considerable value to both pediatrician and dermatologist.

The final section on mastocytosis is particularly timely in view of recent increased interest in mast cell function. The concept of mastocytosis has taken a long time to develop, and represents a logical progression from static morphology to functioning system pathology. Urticaria pigmentosa has been known as a skin disease for almost 100 years, but the concept of mastocytosis was not enunciated until 1936, and most of the progress in this subject has occurred in the past ten years. A good deal of the recent advance in knowledge has been due to the author's efforts, and his presentation is authoritative. This section provides useful information for any clinician interested in mast cell diseases.

The volume is illustrated throughout in black and white. Clinical photography is adequate in amount and is well done, but the quality of microphotography is variable. Perhaps the main deficiency is in lower power photographs, which illustrate neither cellular detail nor distribution of microscopic changes.

(Continued on page 1102)

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1. Southam, A. L.: Dysfunctional Uterine Bleeding in Adolescence, Clin. Obst. & Gynec. 3:241 (March) 1960.

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(Continued from page 1100)

LIVER CIRRHOSIS MORTALITY AS A MEANS TO MEASURE THE PREVALENCE OF ALCOHOLISM. Kettil Bruun, Esko Koura, Robert E. Popham and John R. Seeley. 115 pp. The Finnish Foundation for Alcohol Studies, Helsinki, 1960. Cloth-bound $3.00. Paper-bound $2.50.

The Jellinek Alcoholism Estimation Formula is a method by which the number of alcoholics in a given population can be estimated through a study of morbidity and mortality figures. Since our treatment of alcoholism is not as yet sufficiently early and effective, deaths from alcoholic cirrhosis occur in numbers sufficiently large so that the direct relationship between these deaths and the number of alcoholics in the population can be used in order to estimate the prevalence of alcoholism.

Although the Jellinek Formula is more economical and more versatile than a field survey, the accuracy of its results is under constant criticism, and especially by its originator. This text is a study printed in Finnish with an abridged English translation. It is one of many recent attempts to assess the practical value of the formula by other statistical methods. Because of its nature it is highly technical and likely to interest only a select group of students of alcoholism and students of statistical methods, who cannot fail to be impressed by the careful and unbiased work.

Bruun introduces the formula to the reader and discusses its validity in Finland, critically examining each factor in the formula. Koura reports on empirical studies made by himself and Bruun, to determine the P value of the Jellinek Formula for Finland. Popham reports on his investigation of the reliability of reported deaths from liver cirrhosis in Finland in connection with the studies by Bruun and Koura. Seeley contributes some logical comments on the studies. Bruun terminates the book by comparing the results from the Jellinek Formula with an estimate by more direct empirical means, and coming to the same conclusion as other recent studies. The Jellinek Formula tends to give a minimum figure only, the true number of alcoholics being much higher.

TECHNIK DER ROENTGENDIAGNOSTIC (Roentgen Diagnostic Technique). Hanno Poppe, Ilse Lohstöter and Ph. Lauwers. 683 pp. Illust. Georg Thieme Verlag, Stuttgart, West Germany; Intercontinental Medical Book Corporation, New York, 1960. $20.95.

There are only a few textbooks available which deal with radiographic technique. The volume under review is a welcome addition to this somehow neglected branch of radiological literature.

The authors have divided this text into two parts. In the first, they deal with the radiographic technique of all diagnostic procedures. The anatomy of the radiographed sections is presented in detail, followed by photographic reproductions of the respective positions and the radiographs thus obtained. There are graphic data and illustrations with each procedure, giving the size of the film, focus film distance, the use of screens and of the grid, and the technique for a four-valve and six-valve generator. The centre point is shown on a photograph of the subject. Thus the most detailed data pertaining to the taking of radiographs are given.

The first part is divided into chapters, each of which deals with a separate part of the body. Special procedures such as bronchography, tomography and kymography are also well described. In the section on x-ray technique of the urinary tract, pneumopyelography, ureteropneumography and pneumoperitoneum and retroperitoneum air insufflation are described. A separate chapter is devoted to the angiographic procedures, including splenoportography, aortography and arthrography. In forty pages, the medical terminology as applied to radiographic procedures is provided.

The second part of this textbook is devoted to the physics and technology of the roentgen ray. It begins with a short biographical sketch of Wilhelm C. Roentgen. This is followed by an introduction to the physics of electricity, ionization, the vacuum tube and the spectrum of the roentgen rays; a discussion of the technology of x-ray tubes and x-ray generators and controls, specialized equipment for tomography, the physics and technique of the x-ray image and the various techniques connected with it, x-ray protection, intensifying screens, sensitimetric studies and darkroom technique; and a review of the most common errors and faults in radiographs.

This is a very desirable book. Its language is simple and the photographic demonstrations make the procedures self-explanatory. The authors are to be congratulated on the excellence of the text and the great care they have taken in the preparation of this book, which will be welcomed by radiographers and radiologists in many parts of the world.

The publishers deserve high credit for the graphic qualities of this book.

A SYNOPSIS OF CONTEMPORARY PSYCHIATRY. 2nd ed. George A. Ulett and D. Wells Goodrich. 309 pp. The C. V. Mosby Company, St. Louis, Mo., 1960. $6.50.

This handbook was intended to fill the need for a brief text of psychiatry as a quick reference for medical and psychological interns, medical students, psychiatric residents during the first period of their residency, nurses and others working in psychiatric hospitals and clinics, and, last but not least, for the general practitioners who are increasingly becoming aware of the need to deal with psychiatric problems in everyday practice. The authors are to be commended for the way they have successfully filled this need. The wealth of material they succeeded in offering in a readable presentation and in a book small enough to fit in the side pocket of a clinic coat is remarkable. The content is distinctly divided in three general areas: Part 1, history taking and diagnostic procedures; part 2, clinical syndromes; and part 3, therapeutic measures. The authors' approach is an eclectic one and they seem to have selected the most important and least debatable information in a manner showing great practical and pedagogical experience. Recent information on psychotropic drugs is given in clear tabular form. Theory is kept to a minimum; however, each chapter is completed by a carefully selected list of publications for suggested reading.

This synopsis of contemporary psychiatry is not intended to replace large textbooks but can be warmly recommended for those purposes and groups of interested readers whom the authors had in mind to serve.

(Continued on page 1104)

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1. Meyers, G. B.: Ind. Med. & Surg. 26:3, 1957. 2. Murray, R. J.: N. Y. St. J. Med. 53:1867, 1953.

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(Continued from page 1102)

INSTRUCTIONAL COURSE LECTURES 1960. THE AMERICAN ACADEMY OF ORTHOPAEDIC SURGEONS. Edited by Fred C. Reynolds. 420 pp. Illust. The C. V. Mosby Company, St. Louis, Mo., 1960. $18.50.

At its annual convention, the American Academy of Orthopaedic Surgeons conducts a series of instructional courses designed to bring practising orthopedists up-to-date in selected fields. The substance of the new courses for each year is published in book form.

The 1960 volume is the 17th to be published, and maintains the standards of its predecessors. There are five parts to this volume, segregated under the following headings: Fractures, Bone Graft Surgery, Children's Orthopedics, Athletic Injuries, and Miscellaneous. As might be expected in a book of this sort, the authors avoid contentious or extremely new techniques, and describe only those methods which they have found to be satisfactory. This results in useful summaries of current practice in various fields, and gives the book its reputation as the vademecum of senior orthopedic residents on this continent. Of particular interest in this year's volume are the symposia on femoral neck fractures and on athletic injuries. While neither type of injury is new or uncommon, it is refreshing to have the views of several recognized authorities assembled together in the same volume.

THE NATIONAL LIBRARY OF MEDICINE INDEX MECHANIZATION PROJECT. Bulletin of the American Library Association, Vol. 49, No. 1, Part 2. Edited by Seymour I. Taine. 96 pp. Illust. National Library of Medicine, Washington, D.C., 1961. $2.00.

Basic periodical indexes, covering broad areas of the sciences, to be of the greatest service to searchers, require a comprehensive listing of the material and prompt publication. The new "Index Medicus" aims to combine these two fundamental characteristics in the one publication. This report, published as Part 2 (of 2 parts) of the January 1961 issue of the *Bulletin of the Medical Library Association*, is a detailed description of the choice of equipment, the processing of the material and the operational history of the project undertaken by the National Library of Medicine in the production of the new "Index Medicus" during its first year, 1960.

Improvements in the "Current List" had been under consideration for some time before the "Quarterly Cumulative Index Medicus", published by the American Medical Association, ceased publication in 1959. These included numerous technical refinements in processing and also factors of user interest, such as currency of material, legibility, more convenient searching methods and a better coverage of medical periodicals. To a great degree these objectives have been achieved and other special projects are under consideration, such as an efficient reference and bibliographic service. "Index Medicus", now the largest indexing service in any subject field, at a subscription rate of $20.00 per year for 12 issues, furnishes information to its subscribers at a cost of less than $.0002 per article indexed. On the average, this information is available to the subscriber about ten weeks after publication of the periodical. It covers 1700 English and foreign journals and, in 1960, indexed an estimated 125,000 articles using 5000 main subject headings and 67 standard topical subheadings. For those who desire a cumulative volume, an annual "Cumulated Index Medicus" will be published by the American Medical Association in collaboration with the National Library of Medicine. This permanent reference tool will contain over 4000 pages and will be issued in several volumes.

Users have generally been pleased with the new format, which eliminates the two-step shuttling back and forth from section to section, but some lament the demise of the Register of Articles, one feature of the "Current List" which served as a target for adverse criticism over the past decade. A study of this comprehensive report, outlining the scope of the undertaking and revealing the evident skill and foresight displayed by those responsible for the project in overcoming the many problems encountered in production, leaves little room for criticism.

SPEECH THERAPY IN CEREBRAL PALSY. American Lecture Series. Merlin J. Mecham, Martin J. Berko and Frances Giden Berko. 307 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1960. $11.00.

This interesting and well-written work has the advantage of being the product of three authors each of whom has had extensive experience in some contributory phase of habilitation of the cerebral-palsied. It is well documented with references from a wide variety of sources, and the manuscript was reviewed by eminent authorities in cerebral palsy. It, therefore, fills a need for those who teach in this field and for students of this subject. Cerebral palsy creates such a wide variety of disorders that those engaged in any of the restorative functions must acquire a solid knowledge of its complexities. Introductory chapters of the volume cover this principle. In a logical fashion the book proceeds from there to ask the questions that plague us all and, in as far as possible from present-day information, reveals the answers.

Those who toil in this unrewarding vineyard are more inclined to wonderment at success than to astonishment of failure. There are ten good reasons for failure that can easily be produced where speech problems accompany cerebral palsy. This would be pleasant and informative reading for the student in speech therapy were it not for the appendices. With these added, it becomes a true source of inspiration.

THE PATHOLOGY OF CEREBRAL PALSY. Abraham Towbin. 206 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1960. $8.75.

This monograph of some two hundred pages is somewhat disappointing. It suffers from too frequent use of the term cerebral palsy as though it were a disease entity. It is not a term that one would expect a pathologist to use. There is no specific disease or condition called cerebral palsy. The pathological conditions that cause motor disorders cannot be separated from general neuropathology. The author excludes neurological disorders acquired after the age of two. Does not the child who develops a hemiplegia after an infectious disease have a type of cerebral palsy? The correlation between the clinical state and the pathology described could be improved.

Those interested in learning about neuropathology of motor disorders in children would not receive much help here and are advised to consult one of the more standard textbooks on neuropathology.

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RESIDENT IN ANESTHESIA WANTED July 1, 1961, for the recently reconstructed 270-bed Queen Elizabeth Hospital of Montreal. Approved for postgraduate training by the Canadian, American and British authorities. Stipend varies with the experience of the applicant from $175 to $300 per month, plus room and board or living-out allowance. Apply to Dr. W. G. Cullen, Anesthetist-in-Chief, 2100 Marlowe Avenue, Montreal 28, Quebec.

RESIDENT IN RADIOLOGY, first year, wanted for July 1, 1961 or January 1, 1962 for a 480-bed new medical centre affiliated with medical school. Stipend $250 first year, $275 second year, $375 third year per month with room and laundry. For particulars apply to Dr. Julian O. Salik, Sinai Hospital of Baltimore, Inc., Greenspring at Belvedere, Baltimore 15, Maryland, U.S.A.

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MEDICAL NEWS *in Brief*

(Continued from page 1084)

MONTREAL GENERAL HOSPITAL "ALUMNI AT HOME"

The Montreal General Hospital announces that an At Home for members of the medical and dental professions who have been associated with the hospital on the intern or attending staff will be held immediately after the 1961 national annual meeting of the Canadian Medical Association in Montreal in June.

The At Home program will comprise a dinner at the Queen Elizabeth Hotel on Friday, June 23, and a wide variety of functions at the hospital on Saturday morning, June 24, including selected operations, demonstrations in the new surgical and medical research laboratories, clinical demonstrations in the dental department, tours of the hospital and an informal reception in Livingstone Hall concluding at noon.

Dr. S. A. MacDonald, Chairman of the At Home Committee, informs the Journal that the dates and the program have been selected so as to complement but not duplicate or interfere with Canadian Medical Association sessions, and to enable all M.G.H. Alumni attending the C.M.A. meeting to renew acquaintances with their fellow graduates as well as to observe the tremendous recent developments in the Hospital, and that the C.M.A. graciously extends an invitation to M.G.H. Alumni who are not C.M.A. members to attend the technical and social sessions of its annual meetings which conclude on the afternoon of Friday, June 23.

Alumni At Home registration desks will be set up in the Queen Elizabeth Hotel and at the hospital during the C.M.A. meeting where those who wish to participate may obtain full information and register for all or part of the At Home program.

EXPERIMENTAL TRANSPLANTATION OF AUTOGENOUS JOINTS

Study of free transplantation of joints is of extreme importance as a means of reconstruction of injured or deformed joints, such as the hand and temporomandibular joints. At the Montreal Physiological Society Meeting, December 1, 1960, Entin and Baird reported on experiments designed to evaluate the effect of various factors contributing to the success of autogenous joint transplantation in animals. In a group of 82 dogs, the metacarpophalangeal joint was utilized and the effect of size, location, duration of follow-up and other factors was noted. The final assessment consisted of clinical observation of general appearance, gait, range of passive movement and correlation with x-ray appearance and macroscopic studies. The following morphological changes were noted: narrowing of the joint, widening of the bone, cartilaginous degeneration, fragmentation of adjacent bone, invasion of fibrous tissue into the joint space and complete destruction of the architecture of the joint. There was no consistent correlation between the clinical result and the actual anatomical state of the joint. Similar observations were noted in a small

group of transplanted joints in man. In both groups the morphological changes after long-term follow-up were suggestive of the degenerative processes associated with various types of arthritis in man.

CIRCULATION SUSPENDED FOR 32 MINUTES

The entire circulation of a 2-month-old 6-lb. boy was suspended for 32 minutes recently while surgeons performed a successful operation for total anomalous pulmonary venous drainage. The heart surgery team at the Children's Hospital, Buffalo, reduced the infant's temperature to 14° C. in two minutes by means of a heat exchanger connected to a blood pump. At 20° C., heart action ceased. After holding the temperature constant at 14° for seven minutes to allow all the organs to cool, circulation was stopped. Tubes connecting the blood pump to cannulae in the right atrium and the arch of the aorta were clamped off, and tapes were placed around the superior and inferior venae cavae to prevent seepage of the blood in those vessels into the atrium.

The infant's pulmonary veins emptied into a much-enlarged coronary sinus instead of into the left atrium. The only blood reaching the left side of the heart was that escaping through the foramen ovale, which was about 2 cm. in diameter. The existing atrial septum was excised and the two atria were redivided with a 3½-cm. patch of teflon cloth, so that the coronary sinus would open into the left instead of the right atrium. The opening of the coronary sinus was enlarged. As a result, blood flowing from the pulmonary veins into the coronary sinus was directed into the left atrium in the normal manner. The amount of coronary blood coming through the sinus is so slight that its mixture with the oxygenated blood being pumped out of the heart was deemed by the team to be of small moment. The right atrium was filled with blood, the incision closed, the tapes removed from the venae cavae, and the clamps taken off cannulae leading to the blood pump. As the circulation through the pump resumed, the blood was rapidly rewarmed. A defibrillator steadied the heart to a normal rhythm as it resumed beating.

Members of the team were Drs. N. B. Thomson, Jr., surgeon, and E. C. Lambert and Peter Vlad, cardiologists, all of the University of Buffalo Medical School faculty.

A NEW RENAL TUBULE AMINOACID TRANSPORT SYSTEM

Reabsorption of aminoacids from glomerular filtrate during its passage through the proximal renal tubule probably requires active transcellular transport systems. One such system has been suggested for the common reabsorption of cystine, lysine, arginine and ornithine (*Clin. Sc.*, 16: 75, 1957). At the Montreal Physiological Society Meeting, December 1, 1960, Scriver and Schafer reported on studies which seem to demonstrate another common transport system in the renal tubule that involves glycine, proline and hydroxyproline. By means of rapid intravenous in-

(Continued on page 32)

MEDICAL NEWS *in brief*

(Continued from page 31)

fusion of L-proline in normal subjects, the renal clearances of glycine and hydroxyproline were immediately and temporarily increased six fold or more; plasma levels of these two aminoacids were not significantly altered; proline excretion was greatly increased during this period. Complementary but less dramatic results were obtained with equimolar (43.5 mM) glycine infusions. Interpretation of the data suggests that glycine has a lower affinity for the common transport mechanism than the other two aminoacids. Supportive evidence for the presence of this particular transcellular transport system was found in aminoacid clearance studies in three clinical disorders (hyperprolinemia, Hartnup disease and osteomalacia with increased glycine clearance). The methods used were two-dimensional filter paper partition chromatography, combined ionophoresis and partition chromatography on paper and quantitative aminoacid analysis on cation exchange resin.

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U.S. HEALTH GOALS FOR THE 1960'S

Five major health goals of the United States in the 1960's have been projected by an advisory committee to the White House Commission on National Goals. The committee, headed by Dr. James P. Dixon, president of Antioch College, and including Drs. Michael E. DeBakey, of Baylor University College of Medicine, and Harold M. Marvin, of Yale University School of Medicine, set these objectives.

1. Extension of basic medical services to millions not now covered, through expansion of community facilities, more efficient utilization of general hospitals as community health centres, and broadening of group practice.

2. Expansion of rehabilitation services through increases in public funds and voluntary health insurance.

3. Broadening medical care for the aged, a need arising out of "the victories of medicine and public health over the infectious diseases, especially of childhood", and as a consequence of the rising standard of living.

4. Accelerating research into the causes and cures of mental illness, including an expansion of voluntary health insurance to cover some forms of treatment and an enlargement of community health facilities to assume some of the care of patients discharged from mental hospitals.

5. Taking steps to inform the public about health matters and "to improve the general health knowledge of each person . . . to recognize the relationship of environment to health, and to understand that one's genetic inheritance, family relationships and even job situation may influence both physical health and health of the mind".

The advisory committee's report, written by Dr. Dixon, noted that more than $55 billion is being spent annually for health and welfare services in the U.S., accounting for about 12% of the gross national product.

—

ENZYMES SEEN AS CLUE TO ORIGIN OF SPECIES

A highly refined system based on enzyme structure can be used to classify living organisms. Dr. N. O. Kaplan of Brandeis University states that even bacteria can be classified by their enzyme structures as well as by conventional measurements related to overall physical structure and function.

Reporting his findings before a conference on enzymes sponsored by the New York Academy of Sciences, he said that there were marked differences between enzymes from invertebrates and those from vertebrates. Evidence has also shown that changes in enzyme structure may have been significant in the establishment of new species.

Enzymes vary significantly in structure even though they may carry out the same functions. Until recently it was believed that enzymes which mediated the same reactions possessed identical structures. It has now been found that enzymes arising in heart, muscle, liver or kidney tissue, although playing identical roles in body chemistry, are actually different in structure.

Further, enzymes are not only species-specific but also tissue-specific. Dr. Kaplan's work demonstrates that enzyme differences between species and even within species are striking and biologically

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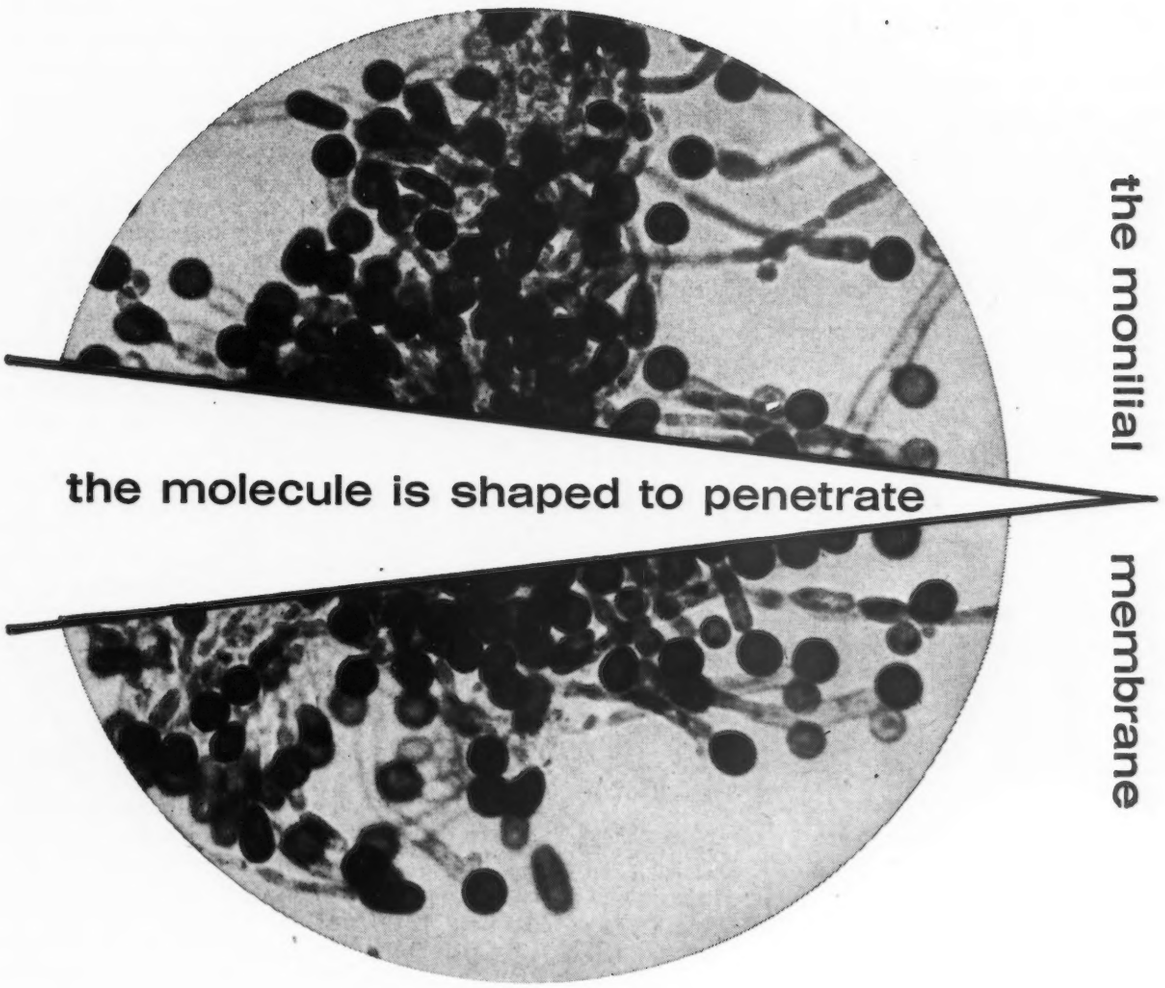
FOR MONILIASIS



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*Trade Mark

†Lapan, B.: Am. J. Obst. & Gynec. 78:1320, 1959.

MEDICAL NEWS *in brief*

(Continued from page 32)

reliable. Because of their characteristic individuality, enzymes offer a valuable approach to the study of species interrelationships and origins. – New York Academy of Sciences.

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1961 CIBA MEDICAL RESEARCH FELLOWSHIP

The CIBA Medical Research Fellowship for 1961 has been awarded to Ingeborg Radde, M.D., Ph.D., F.R.C.P.[C], of Toronto. Dr. Radde, who brings a distinguished medical background to her appointment, will undertake a research project dealing with thyroid physiology, and will work at Queen's University under the direction of Dr. D. L. Wilson.

—

CATASTROPHE DEATHS

Catastrophes–accidents in which five or more persons are killed–caused somewhat over 1400 deaths in the continental United States in 1960, or about the same number as in 1959, according to the Metropolitan Life Insurance Company.

In the year just ended there were eight major catastrophes – those which took the lives of at least 25 persons – accounting for approximately 450 deaths.

The worst disaster of the year was the mid-air collision between two scheduled planes over Staten Island, N.Y., on December 16, causing 134 deaths (including casualties on the ground) – the heaviest loss of life in aviation history.

Other major catastrophes included the explosion of a scheduled plane in flight near Tell City, Ind., on March 17, taking 63 lives; the plane crash into Boston Harbor on October 4, killing 62 persons; the crash of an air liner into a swampy ravine near Richmond, Va., on January 18, causing 50 deaths; the "disintegration" in flight near Wilmington, N.C., of a plane on January 6, killing 34 persons; and a fire which swept an aircraft carrier in Naval Shipyard at Brooklyn, N.Y., on December 19, taking 50 lives.

There were two natural disasters during 1960: Hurricane Donna, which struck the south and northeast in September, causing 30 deaths; and the series of tornadoes which killed 29 in Oklahoma and Arkansas on May 5.

Motor vehicle accidents accounted for nearly one-third of the lives lost in catastrophes last year, and civil aviation was responsible for almost as many deaths. Fires and explosions–most of them in the home–caused about one-fifth of all fatal injuries sustained in catastrophes. Natural catastrophes, military aviation, and water transportation contributed appreciably to the total.

Among catastrophe deaths, civil aviation took a much larger toll than in 1959, while military aviation showed a more moderate rise. On the other hand, there was a decline in catastrophic deaths in motor vehicle accidents, fires and explosions, water transportation, and railroad accidents.

—

THIRD WORLD CONGRESS OF PSYCHIATRY

The Organizing Committee of the Third World Congress of Psychiatry which will be held in Montreal, June 4 to 10, 1961, announces the following features of the Congress program.

SUNDAY, JUNE 4 — Registration

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MEDICAL NEWS *in brief*

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MONDAY, JUNE 5

Morning.—Opening ceremonies with addresses by various dignitaries.

Afternoon.—The first plenary address on Phenomenology will be delivered by Dr. H. C. Rumke (Holland), the second by Professor Jules Masserman (U.S.A.) on Experimental Aspects of Psychiatry, and the third by Dr. Henri Ey (France) on the Theories of Psychiatry. Simultaneous translation into the four official languages of the Congress (French, German, Spanish, English) will be available during these sessions.

Evening.—Dr. Max Fink (New York) will chair a meeting on Electroencephalographic Changes in Human Psychopharmacology.

TUESDAY, JUNE 6

Morning.—The morning program will open with a plenary session on Mental Hospitals, featuring an international list of speakers. Professor K. Leonhard (East Berlin) has organized a panel on Atypical Endogenous Psychoses; a session on Forensic Psychiatry has been organized by Professor M. Remy (Switzerland); and Dr. Paul Hoch (U.S.A.) will chair the third panel of the morning on Pseudoneurotic Schizophrenia. A panel discussion on Medical Psychology will be chaired by Professor Joseph Zubin (New York).

Afternoon.—A plenary session on Neurophysiology will feature important papers by outstanding workers in this field. Two panels have been scheduled for the afternoon, the first on Addiction, organized by Drs. J. V. Lowry and M. A. Diamond, (U.S.A.), who will chair an international panel. Dr. P. J. van der Leeuw (Amsterdam) will lead the second panel on Psychoanalysis. During the afternoon there will be panels on Experimental Psychopathology chaired by Professor L. J. West (U.S.A.); Psychiatric Occupational Therapy, led by Dr. P. C. Sivadon (France); and a sub-section on Forensic Psychiatry will be held with subsequent sessions on Wednesday and Thursday afternoons. One of the highlights of the afternoon will be a special panel on the Planning of National Psychiatric Programs chaired by Dr. R. H. Felix, former president of the American Psychiatric Association.

Evening.—Several discussion groups have been organized, one on Experimental Psychopathology, Religion and Psychiatry chaired by Dr. G. C. Anderson (U.S.A.), another on Abolishing Mental Hospitals by Dr. F. Bierer (England), and the third on the Association for the Advancement of Psychotherapy with Dr. S. Lesse (U.S.A.) in the chair.

WEDNESDAY, JUNE 7

Morning.—Wednesday morning will be devoted to academic and key lectures by Professor J. Piaget (Switzerland) and Dr. H. W. Magoun (U.S.A.).

Afternoon.—The afternoon will begin with a plenary session on Child and Family Psychiatry. The session on Sensory Isolation is being organized by Dr. Philip Solomon (Boston). This is of special concern in regard to space flights. The panel discussion on Psychosomatics is being chaired by Professor C. A. Seguin (Peru). Psychotherapy of Psychoses will be dealt with by Professor G. Benedetti (Switzerland), and a group

(Continued on page 41)

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K.C. Rodger, M.D.,
R.W. Lee, M.D.,
Edna E. Power, B.A.,

Canadian Medical Association Journal
83,991-996 Nov. 5, 1960

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MEDICAL NEWS *in brief*

(Continued from page 37)

on Existential Psychiatry is being organized by Dr. J. M. Scher (Chicago).

Evening.—An unprecedented discussion by three Nobel Prize winners, on Scientific Creativity, will highlight the evening session. The three discussants are Lord Adrian, Dr. Albert Szent-Györgyi and Dr. Linus Pauling.

THURSDAY, JUNE 8

Morning.—Professor Jean Delay (France) will chair a panel discussion on Psychopharmacology. Professor H. Ehrhardt (West Berlin) will lead a discussion on Juvenile Delinquency, and leading authorities will discuss and examine the role of the Psychiatric Nurse. The plenary session on Psychotherapy will feature a distinguished list of speakers.

Afternoon.—A plenary session will be held on Physical Therapies. Corticovisceral Mechanisms will be discussed by a distinguished group of Russian psychiatrists and by Dr. W. H. Gantt (Baltimore). Family Psychiatry, another panel discussion, is being organized by Dr. N. W. Ackerman (New York), and Autogenic Training by Professor Schultz (Germany) and Dr. W. Luthe (Montreal). Seven subsections of Psychopharmacology have been scheduled.

FRIDAY, JUNE 9

Morning.—Social Psychiatry will lead off the plenary session. A panel discussion on Mental Retardation is being organized by Professor H. Asperger (Austria). Training in Psychiatry and Social Therapy and Aftercare will be chaired by Dr. J. Whitehorn (U.S.A.) and Dr. W. Barton (Boston), respectively. A number of papers on Psychopathological Art have been grouped for presentation.

Afternoon.—A plenary session on Concepts and Methods will be followed by panels on Geriatrics and Child Psychiatry chaired respectively by Dr. Martin Roth (England) and Dr. Serge Lebovici (Paris). Dr. A. Stein (New York) will lead a discussion on Group Psychotherapy and a panel chaired by Dr. E. Jacobsen (Denmark) will deal with Alcoholism. A third discussion, on Community Mental Health, has also been scheduled.

SATURDAY, JUNE 10

Morning.—Saturday morning will provide an outstanding plenary session on Psychopathology. Panel discussions, on Transcultural Studies, The Therapeutic Community, Psychoendocrinology, and Sleep and Dreams will be led by Dr. Alexander Leighton (New York), Dr. Maxwell Jones (U.S.A.), Dr. R. A. Cleghorn (Montreal), and Professor Nathaniel Kleitman (U.S.A.), respectively.

CANADIAN ASSOCIATION OF PATHOLOGISTS

The Canadian Association of Pathologists will meet in Montreal from June 22 to 24, 1961. The Association's Business Meeting will take place on Thursday evening, June 22, in the amphitheatre of the Montreal Children's Hospital. Scientific sessions will be held on Friday, June 23, and Saturday, June 24, in the auditorium of the Hôtel-Dieu Hospital, Montreal.

(Continued on page 43)

New!

THE McCARTHY INFANT ELECTROTOME

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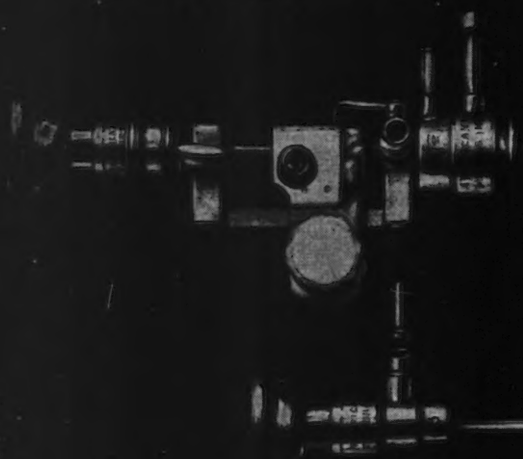
ACCESSORY VEST MINIATURE FORWARD VISION and MEADS RIGHT ANGLE TELESCOPE

These miniature telescopes were devised for use with the McCarthy infant electrotome sheath for examination before or after transurethral operations. They are important additions to the instrumentarium of the urologist practicing pediatric urology.



The McCarthy Infant Electrotome. The telescope is an extremely small foroblique optical system. The instrument is of inestimable value for contracture of the vesical orifice, small bars of the vesical orifice and excising congenital valves of the urethra. Cat. No. 4545

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The optical system of the Meads Telescope permits a right angle visual field. The telescope was designed for examination before or after transurethral resection. It also permits single ureteral catheterization. A deflector at the distal end aids in the accurate placement of the catheter. Cat. No. 4546

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MEDICAL NEWS *in brief*

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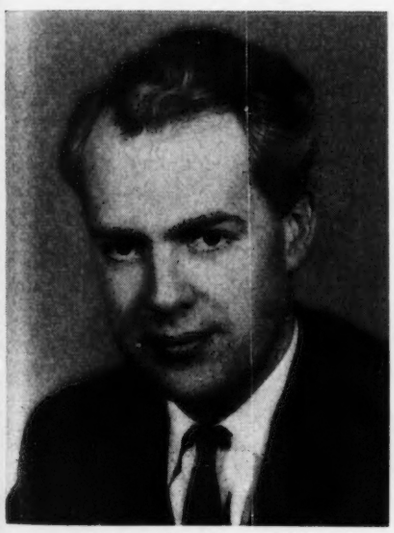
QUEEN ELIZABETH II CANADIAN FUND: 1961 AWARDS FOR RESEARCH ON CHILDREN'S DISEASES

Appointment of the first "Queen Elizabeth II Scientist" has been announced by the Board of Trustees of the Queen Elizabeth II Canadian Fund to Aid in Research on the Diseases of Children. The recipient is Dr. Michael W. Partington, 34, a research fellow in neurology at the Research Institute of the Hospital for Sick Children, Toronto. Dr. Partington will take up his new post on July 1, 1961, in the Department of Pediatrics at Queen's University, Kingston, where a permanent research unit will be set up to initiate, foster and carry out research on pediatric problems such as mental deficiency and epilepsy.



Dr. M. W. Partington

Three "Queen Elizabeth II Fellowships" totalling $13,500 were also awarded to:

Dr. John Alexander Lowden, 27; renewal of Fellowship, to continue studies towards Ph.D. degree in biochemistry at McGill University, under Drs. K. A. C. Elliott and L. S. Wolfe.

Dr. George Greenough Hinton, 35, research fellow in neurology at London, England, to work at the War Memorial Children's Hospital and the Psychiatric Research Centre, London, Ontario, under Drs. J. C. Rathbun and D. Zarfas.

Dr. Hugh Taylor, 30, Chief Resident of the Children's Hospital, Winnipeg, to work in the Department of Pediatrics, New York University, under Drs. J. Dancis and S. Krugman.

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CANADIAN ACADEMY OF ALLERGY

The 1961 Annual Meeting of the Canadian Academy of Allergy will be held at the Mont Tremblant Lodge Club, Mont Tremblant, Que., on June 18, 19 and 20. Scientific sessions will be held on the mornings of Monday, June 19 and Tuesday, June 20, the afternoons of these days being reserved for recreation (golf, fishing, water skiing). The annual business meeting of members and the election of the Executive will be held on June 19, at 5 p.m., followed by a dinner at 8 p.m. On Wednesday morning, June 21, a round-table panel on "Allergy and Collagen Diseases" will be presented. Further information from: Dr. H. L. Bacal, Secretary-Treasurer, 4640 Stanley Weir, Montreal, P.Q.